A FUNDAMENTAL STUDY OF THE AIRFLOW AND ODORANT TRANSPORT PHENOMENA OF CANINE OLFACTION

A Dissertation in

Mechanical Engineering

by

Michael J. Lawson

© 2010 Michael J. Lawson

Submitted in Partial Fulfillment
of the Requirements
for the Degree of

Doctor of Philosophy

December 2010
The dissertation of Michael J. Lawson was reviewed and approved* by the following:

Gary S. Settles  
Distinguished Professor of Mechanical Engineering  
Dissertation Adviser  
Co-Chair of Committee

Eric G. Paterson  
Professor of Mechanical Engineering  
Co-Chair of Committee

Karen A. Thole  
Head of the Department of Mechanical and Nuclear Engineering

Robert F. Kunz  
Professor of Aerospace Engineering

* Signatures are on file in the Graduate School
ABSTRACT

Olfaction begins when an animal draws odorant-laden air into its nasal cavity by sniffing, thus transporting odorant molecules from the external environment to olfactory receptor neurons (ORNs) in the sensory region of the nose. The dog and other macrosmatic (keen-scented) mammals have evolved a complex nasal anatomy that facilitates the efficient aerodynamic sampling of inspired odorant molecules. Here, airflow and odorant transport patterns in the canine nasal cavity are studied through a set of flow visualization experiments and computational fluid dynamics (CFD) simulations.

An anatomically-correct experimental model of the canine nasal cavity, based on high-resolution magnetic resonance imaging scans, was designed and fabricated using a rapid prototyping technique. Dye-injection flow visualization experiments were performed using this model to characterize the canine’s internal nasal airflow patterns. The results from these experiments illustrated the complex three dimensional flow patterns throughout the nasal cavity. The experimental results also confirmed the existence of distinct olfactory and respiratory airflow paths and were used to study the transition between laminar and turbulent flow domains. Moreover, these experiments were used to both qualitatively and quantitatively validate previous and current CFD simulations of canine nasal airflow.

Steady and unsteady CFD simulations of odorant transport and deposition in the nasal cavity were performed. The simulations modeled the transport of odorant from the external environment, through the nasal airways, across the olfactory mucus layer, and
to ORNs sites. Steady simulations were performed to study the relationship between odorant solubility and odorant deposition patterns (i.e. odorant flux patterns) across the canine’s olfactory region. Highly-soluble odorants were deposited mainly along the entrance to the olfactory region. Moderately-soluble and insoluble odorant fluxes to the olfactory epithelium are significantly lower than those for highly-soluble odorants. However, these less soluble odorants are deposited more uniformly across the olfactory epithelium. The canine’s nose apparently utilizes odorant absorption over a large surface area to compensate for the lower absorption rate of insoluble odorants.

Physiologically-realistic sniffing was simulated to examine the effects of unsteady airflow on odorant transport. The unsteady simulations showed that the airflow is unidirectional in the olfactory region during inspiration and stagnant on expiration. Unsteady odorant transport patterns for highly-soluble and moderately soluble odorants were observed to become temporally fully-developed after a single sniff. Accordingly, the steady and unsteady odorant deposition patterns are qualitatively similar for these odorants. Insoluble odorant transport and deposition patterns however continue to develop over the course of many sniff cycles.

This work shows that the canine has evolved a complex nasal anatomy that creates odorant-specific deposition patterns. These patterns allow the canine’s nose to separate the components of a complex scent, as in chromatography, in order to possibly improve neurological olfactory pattern recognition. The lessons learned on efficient aerodynamic sampling techniques are also used to suggest biomimetic design principles to improve artificial olfaction devices.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Tables</td>
<td>xiii</td>
</tr>
<tr>
<td>List of Figures</td>
<td>xiv</td>
</tr>
<tr>
<td>Chapter 1. Introduction and literature review</td>
<td>1</td>
</tr>
<tr>
<td>1.1 Introduction</td>
<td>1</td>
</tr>
<tr>
<td>1.2 Literature review</td>
<td>3</td>
</tr>
<tr>
<td>1.2.1 The canine nasal anatomy</td>
<td>3</td>
</tr>
<tr>
<td>1.2.1.1 Histology</td>
<td>6</td>
</tr>
<tr>
<td>1.2.1.2 Respiratory mucosa</td>
<td>7</td>
</tr>
<tr>
<td>1.2.1.3 Olfactory mucosa</td>
<td>8</td>
</tr>
<tr>
<td>1.2.1.4 Olfactory receptors</td>
<td>9</td>
</tr>
<tr>
<td>1.2.2 The physical phenomena of odorant transport during canine olfaction</td>
<td>11</td>
</tr>
<tr>
<td>1.2.3 Studies of nasal airflow</td>
<td>13</td>
</tr>
<tr>
<td>1.2.3.1 Experimental</td>
<td>13</td>
</tr>
</tbody>
</table>
Chapter 2. Flow visualization experiments to describe canine nasal airflow

2.1 Materials and methods

2.1.1 Creating an anatomically-correct experimental model of the canine nasal cavity

2.1.1.1 Determination of the scale of the experimental model

2.1.1.2 Selection of a RP technique

2.1.1.3 Experimental model design and fabrication

2.2 Experimental methods

2.2.0.4 Flow rate and pressure loss scaling
2.2.0.5 Experimental setup ........................................ 30
2.2.0.6 Velocimetry measurement technique ..................... 31
2.3 Results .................................................................. 34
  2.3.1 Inspiratory nasal flow patterns ............................. 35
    2.3.1.1 Influence of the nasal flow rate on inspiratory flow patterns ........................................ 38
    2.3.1.2 Effect of the dye injection location on the dye flow path during inspiration .................... 40
    2.3.1.3 Velocimetry measurements .............................. 40
    2.3.1.4 Airflow residence time in the olfactory region .... 43
  2.3.2 Expiratory nasal flow patterns ............................... 45
  2.3.3 Airflow resistance measurements ............................ 47
2.4 Discussion ............................................................ 47
  2.4.1 Comparison of experimental results to previous CFD simulations .................................... 47
2.5 Summary ............................................................... 50

Chapter 3. A mathematical model for odorant transport during olfaction .......................... 52
  3.1 Governing equations .............................................. 52
3.1.1 Advective-diffusive transport in the nasal airways 53
3.1.2 Odorant transport across the air-mucus interface 54
3.1.3 Odorant transport in the mucus layer 55
3.2 Boundary conditions 56
3.2.1 Airflow boundary conditions 56
3.2.2 Odorant transport boundary conditions 56
3.3 Selection of odorants 59
3.4 Dimensional analysis 61

Chapter 4. Simulating odorant transport during steady inspiration 65
4.1 Materials and methods 65
4.1.1 Generation of an anatomically-correct computational mesh 65
4.1.2 Airflow solution 65
4.1.3 Numerical solution of the mathematical model of odorant transport during canine olfaction 67
4.1.4 Odorant transport boundary condition on olfactory airways 68
4.1.5 Odorant transport boundary condition on respiratory airways 69
4.2 Results

4.2.1 Nasal airflow patterns

4.2.2 Epithelium flux patterns in the canine olfactory recess

4.2.3 The effect of airflow rate on epithelium flux patterns

4.2.4 Comparison of the present results with epithelial flux patterns in the nasal cavity of the rat

4.3 Discussion

4.3.1 Correlation between epithelial odorant flux patterns and ORN expression topography

4.3.2 Relation to behavioral observations

4.4 Summary

Chapter 5. CFD modeling of unsteady odorant transport

5.1 A brief overview of OpenFOAM

5.2 Development of the OpenFOAM application

5.2.1 Simulating airflow and odorant transport

5.2.2 Region coupling algorithm

5.2.3 The mucus-phase grid
5.2.4 Discretization schemes ......................................... 96

5.3 Verification of the OpenFOAM solver ............................ 96

  5.3.1 Verification of the airflow solution .......................... 97

  5.3.2 Verification of air-phase odorant transport ................ 99

    5.3.2.1 Spatial accuracy ........................................... 99

    5.3.2.2 Temporal accuracy ......................................... 101

  5.3.3 Verification of mucus-phase odorant transport ............. 103

  5.3.4 Verification of the air-mucus interfacial boundary condition . 105

Chapter 6. Simulating odorant transport during physiologically-realistic sniffing. 107

  6.1 Methods .......................................................... 107

    6.1.1 Assumptions .................................................. 107

    6.1.2 Boundary and initial conditions ............................. 108

      6.1.2.1 Airflow ................................................... 108

      6.1.2.2 Odorant transport ........................................ 109

  6.1.3 Grid generation ................................................ 111

  6.1.4 Numerical solution ............................................ 112
6.2 Verification . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 113
  6.2.1 Grid dependence study . . . . . . . . . . . . . . . . . . . . . . 113
  6.2.2 Timestep study . . . . . . . . . . . . . . . . . . . . . . . . . . 116
6.3 Results . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 116
  6.3.1 Nasal airflow patterns during sniffing . . . . . . . . . . . . . . 116
  6.3.2 Odorant transport during the sniff cycle . . . . . . . . . . . . . 122
    6.3.2.1 Total odorant flux to the olfactory epithelium . . . . . 122
    6.3.2.2 Detailed odorant transport patterns . . . . . . . . . 123
6.4 Discussion . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 128

Chapter 7. Summary, conclusions, and future research . . . . . . . . . . . . . . . . . . 136
  7.1 Summary . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 136
  7.2 Conclusions . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 137
    7.2.1 Contributions to the basic science of olfaction . . . . . . . . . 137
    7.2.2 Significance to the design of bio-inspired artificial olfaction de-
        vices . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 139
  7.3 Future research . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 141
    7.3.1 Experimental measurements . . . . . . . . . . . . . . . . . . . . 141
    7.3.2 Computational simulations . . . . . . . . . . . . . . . . . . . . . 142
LIST OF TABLES

2.1 The observed range of dye residence times in the olfactory region of the experimental model for the three nasal flow rates considered. The equivalent airflow rates and residence times for a live dog are also presented. 46

3.1 Chemical properties of the odorants presently considered. Partition coefficients were determined using air-water Henry’s Law constants estimated using HENRYWIN version 3.20 (US Environmental Protection Agency, Estimation Program Interface Suite, http://www.epa.gov/oppt/exposure/pubs/episuite.htm). 60

3.2 Fundamental physical variables of odorant transport during canine olfaction. 63

3.3 Nondimensional parameters governing odorant transport in the canine nasal cavity. 64

6.1 Results from the grid dependence study. 114

7.1 Candidate refractive index matching fluids and their properties. Levels of toxicity and flammability are ranked on a scale from 0–5 according to the material safety data sheet (MSDS) for each chemical. 0 is the lowest level. 151
LIST OF FIGURES

1.1 The canine nasal anatomy. Note that the lamina transversa separates the respiratory and olfactory regions, and the two regions are only connected by the dorsal meatus. ................................................................. 4

1.2 Anatomical terms of location in respect to the canine anatomy. ........... 5

1.3 A cross-sectional schematic of the mammalian olfactory mucosa. Adapted from Craven (2008). ................................................................. 8

1.4 Olfactory receptor expression zones in the rat. Each color represents a different expression zone. (Left) A sagittal section of the nasal cavity. (Right) A transverse section of the olfactory region. Adapted from Buck (2005) ................................................................. 10

1.5 Odorant transport phenomena in the nasal airways and the mucus layer. 11

1.6 Representative transverse cross-sections through the nasal cavity of the dog (left) and human (right). Note that the cross-section of the dog’s nose is in the ethmoidal region. The human nasal geometry is reproduced with permission from Liu et al. (2009). ................................................................. 15

2.1 The 4:1 scale experimental model of the canine nasal cavity. .............. 27

2.2 The experimental setup. ................................................................. 30
2.3 (A) An image of dye flow visualization in the respiratory airways of the experimental model captured with the SA-1 high-speed video camera. It is difficult to see the dye-structures because the SA-1 image has poor contrast. (B) The result of processing the SA-1 image in frame A to enhance the contrast of the dye. The dye is visible as the light regions on the otherwise dark background.

2.4 Two sequential SA-1 camera images of dye flow visualization in the experimental model. The dashed boxes show representative interrogation windows used for eddy-velocimetry measurements. The motion of the dye-structures between frames A and B is clearly visible.

2.5 Dye flow visualization in the respiratory airways during inspiration at 50% of the maximum physiological flow rate. (A) A laminar dye streak being injected at the front of the nose. (B) The resulting flow pattern in the respiratory region of the nose. The dashed lines illustrate the observed flow direction of the dye.

2.6 SA-1 camera flow visualization images showing the structure of the flow in the respiratory airways at 15% of the maximum physiological flow rate. (A) The experimental model. The white box indicates the field-of-view for the other images in this figure and the dotted lines delineate the edge of the nasal cavity. (B-D) Sequential flow visualization images in the respiratory airways.
2.7 Olfactory flow patterns on inspiration at 15% of the maximum physiological flow rate. Frames A-D were extracted from D90 camera video recordings at 3, 6, 17, and 40 seconds (equivalent to 0.06, 0.12, 0.33, and 0.77 seconds for airflow in a live dog’s nose) after the initial dye injection. The dashed lines illustrate the general flow direction of the dye in each image.

2.8 A qualitative comparison of experimental and CFD results. (A) A schematic diagram showing the different flow paths observed during dye flow visualization experiments. (B) Streamlines extracted from CFD simulations that were performed using the same nasal geometry (Craven et al. 2009b,a).

2.9 The effect of the nasal flow rate on flow patterns in the nasal vestibule. The field of view for these images is similar to that show in Figure 2.6A. (A) The flow pattern at 15% of the maximum physiological flowrate. At this flow rate, dye mixing is primarily due to laminar mixing and vortex shedding, thus coherent dye-structures are visible. (B) The flow pattern at 100% of the maximum physiological flow rate. At this flow rate, the dye is well mixed near the front of the nasal vestibule by turbulence.

2.10 (A) The computer model of the nostril showing three dye injection locations. (B-D) Dye flow patterns for injection locations 1, 2, and 3, respectively.
2.11 Eddy-velocimetry measurements at several x/L locations along the axis of the dog’s nose at 50% of the maximum physiological flow rate. The x/L coordinate system is defined in Figure 1.1. Measurements were made in the dorsal meatus (top) and the maxilloturbinate airways (bottom). The small square symbols represent individual velocity measurements and the larger triangular symbols represent the average of the velocimetry measurements at the various axial locations. The transverse sections of the nasal geometry illustrate the regions where the velocimetry measurements were made.

2.12 Pressure drop across the experimental model over the full range of physiological flow rates. The pressure measurements were scaled from airflow in the 4:1 scale experimental model to airflow in a live dog’s nose as described in Section 2. The CFD results of Craven et al. (2009b) are shown for comparison. Representative uncertainty bars are shown for both the experimental and CFD data. The uncertainty in the CFD data was estimated using Richardson Extrapolation Analysis (see Craven et al. 2009b).

4.1 The computational domain. The mesh resolution in the respiratory (left) and olfactory (right) regions of the nasal cavity are shown.
4.2 A comparison of odorant concentration profiles of DNT and limonene in a representative transverse cross-section of the olfactory region for deposition Scenarios A and B. The color scales represent the normalized odorant concentration in the nasal airways. Note that the arrows show regions where the concentration profiles were noticeably different. The concentration of DNT in Scenario B was scaled by a factor of 1.9 to account for odorant loss in the dorsal meatus. The concentration of limonene in Scenario B was not scaled because the required scaling factor was approximately 1.

4.3 Inspiratory airflow patterns in the canine nasal cavity at peak inspiration (0.46 L/s). Airflow enters the nose at the left through the nasal vestibule. The red, dark blue, and green streamlines illustrate the dorsal, lateral, and ventral olfactory flowpaths, respectively. The arrow heads on the olfactory streamlines represent the direction of the airflow. The orientation of the nasal cavity is similar to that shown in Figure 1.1.
4.4 Surface contours of odorant flux to ORNs in the olfactory recess in units of $1/m^2\cdot s$ (see Chapter 3) for (a) DNT, (b) amyl acetate, and (c) limonene at peak inspiration (0.46 L/s). The left and right views in each panel show the olfactory recess viewed from lateral and medial perspectives, respectively. Non-olfactory surfaces are colored gray. As shown, the flux to ORNs is non-uniform for (a) DNT and (b) amyl acetate, but it is roughly uniform for (c) limonene. Note that the contour legends vary over four orders of magnitude for the different odorants.

4.5 Transverse contours of nondimensional odorant concentration in the olfactory recess for: (a-c) DNT, (d-f) amyl acetate, and (g-i) limonene. Airflow rates of (a,d,g) 0.05 L/s, (b,e,h) 0.22 L/s, and (c,f,i) 0.46 L/s are shown for each odorant. Note that the left-most transverse slice in each panel contains some non-olfactory airways (see Figure 1.1). Although the concentration in these non-olfactory airways is 1, there is no odorant flux to these surfaces.

4.6 Normalized odorant removal efficiency (Equation 4.4) of the olfactory recess as a function of nasal airflow rate.

4.7 Total odorant uptake by the olfactory recess as a function of nasal airflow rate.
5.1 A simplified schematic of the air-phase and mucus-phase computational domains used to simulate odorant transport in the canine nose. The physical phenomena considered in each domain and at the interfacial surface are listed. $C_{ai}$ and $C_{mi}$ are the air-phase and mucus-phase interfacial odorant concentrations, respectively. ................................. 90

5.2 Flowchart of CSTFoam illustrating the solution algorithm. Here, $n$ is an index that identifies the current sub-iteration loop, $\xi$ is a relaxation factor that is always less than 1, and $\varepsilon^n$ is the error in Henry’s Law at the air-mucus interface. ........................................ 91

5.3 Methods of coupling the air-phase and mucus-phase computational domains. (A) Coupled using a body-fitted mucus-phase grid. (B) Coupled using a mucus-phase grid that is not body-fitted. ............................... 95

5.4 Verification of the airflow solver. .......................... 98

5.5 Boundary conditions for the steady advection-diffusion verification problem. 100

5.6 Verification of the spatial terms in the advection-diffusion equation. . . . 100

5.7 Verification of transient advection in the air-phase. ........................ 102

5.8 Verification of transient diffusion in the mucus-phase. ........................ 104

5.9 Verification of Henry’s Law across the air-mucus interfacial surface. . . 106
5.10 Verification of conservation of mass across the air-mucus interfacial surface. Note that $J^*$ is the nondimensional odorant flux in units of $1/m^2\cdot s$ as defined in Chapter 3. ................................. 106

6.1 Schematic illustration of the computational domain for unsteady odorant transport simulations, showing both the air-phase and mucus-phase boundary conditions. ................................................. 110

6.2 (A) Examples of grid resolution in the dorsal meatus. (B) Respiratory airflow patterns in the maxilloturbinate airways and the dorsal meatus for each grid. (C) Olfactory airflow patterns for each grid. ............ 115

6.3 Time-history of the total nasal airflow rate during the sniff cycle for each timestep considered. Every $15^{th}$ timestep is plotted for $dt = 0.0001$ seconds. ................................................................. 117

6.4 Airflow patterns in the (A) respiratory airways and (B) olfactory airways at peak inspiration (0.05 seconds into the sniff cycle) for each timestep considered. ......................................................... 118

6.5 Time-history of the nasal airflow rate and pressure drop during the sniff cycle. ................................................................. 119

6.6 Contours and vectors of velocity in the z-direction in the dog’s nose during peak inspiration and peak expiration. The dashed lines indicate the general airflow path. Note that the velocity scales are different in the respiratory and olfactory regions. ................................. 121
6.7  (A) Total odorant flux to the epithelium during the sniff cycle for all three odorants.  (B) Total limonene flux to the epithelium on a rescaled y-axis.  

6.8  Transverse cross-sectional contours of odorant concentration in the olfactory region at peak inspiration (0.05 seconds into the sniff cycle) and peak expiration (0.15 seconds into the sniff cycle).  

6.9  The temporal location of the epithelium flux contours presented in Figures 6.10-6.12. The dashed lines A-D correspond to the labels in each figure.  

6.10  Contours of DNT flux across the olfactory epithelial surface. Frames A-D were extracted at times during the sniff cycle identified by the dashed lines in Figure 6.9.  

6.11  Contours of amyl acetate flux across the olfactory epithelial surface. Frames A-D were extracted at times during the sniff cycle identified by the dashed lines in Figure 6.9.  

6.12  Contours of limonene flux across the olfactory epithelial surface. Frames A-D were extracted at times during the sniff cycle identified by the dashed lines in Figure 6.9.  

6.13  Epithelium flux at six different probe locations during the sniff cycle.  (A) The probe locations.  (B) Epithelium flux for probe locations a, b, and c.  

( C) Epithelium flux for probe locations 1, 2, and 3.
7.1 The experimental model of the dog’s nose filled with air, water, and Cargille OHZB fluid. Note that the nose model is made of PolyJet FullCure 720 resin with an experimentally-determined refractive index of $n = 1.530 \pm 0.0025$.

7.2 Results from refractive index matching experiments.
Chapter 1

Introduction and literature review

1.1 Introduction

The dog is one of nature’s best chemical trace detectors, having an olfactory threshold of 1–2 parts per trillion, or roughly 10,000 to 100,000 times lower than that of the human (Walker et al. 2006, 2003; Krestel et al. 1984). Although current artificial olfaction devices are approximately as sensitive as the dog’s nose under laboratory conditions (Moore 2004; Steinfeld and Wormhoudt 1998), dogs easily outperform these man-made devices in “real-world” scenarios where large spaces must be sampled efficiently (Furton and Myers 2001). It therefore seems likely that the dog’s highly-evolved nasal anatomy provides efficient aerodynamic sampling that augments its olfactory abilities.

Olfaction has traditionally been studied by first assuming olfactory receptor neurons (ORNs) have free access to odorant molecules. Only a few studies have considered the critical transport phenomena that deliver odorant molecules to the olfactory region of the nose, and none of these studies have considered the canine. Nevertheless, there is a growing body of evidence that suggests that nasal airflow patterns (Craven et al. 2009a) and odorant deposition patterns in the nasal cavity (Mozell et al. 1991; Kent et al. 1996; Scott et al. 2006; Yang et al. 2007b) play important roles in olfaction. Thus, by studying the characteristics of airflow and odorant transport in the dog’s nose, we can improve our
fundamental understanding of the natural olfactory system while simultaneously learning biomimetic design principles that could be used to improve the performance of artificial olfaction devices.

This dissertation reports the results of a set of experiments and computational fluid dynamics (CFD) simulations that were performed to study the fluid dynamics of the odorant transport phenomena involved in canine olfaction. First, a review of the relevant literature is given in the remainder of this chapter. Chapter 2 presents the results of a set of flow visualization experiments that were performed in an anatomically-correct model of the canine nasal cavity. The experimental results are used to validate previous CFD simulations of nasal airflow and to study flow phenomena, such as the transition between laminar and turbulent flow regimes, that are difficult to investigate with current CFD methods. Chapter 3 presents a mathematical model that was developed to describe odorant transport in the canine nasal airways during olfaction. This mathematical model was solved computationally under two different sets of assumptions. First, CFD simulations were performed using a commercial CFD code under the simplifying assumption that the airflow in the dog’s nose was steady. The results from these simulations are presented in Chapter 4. In actuality, the dog sniffs at approximately 5 Hz (Craven et al. 2009a) during olfaction, resulting in unsteady nasal airflow. Thus, a author-written CFD application was developed to simulate odorant transport in the nasal airways during physiologically-realistic unsteady sniffing. Chapter 5 describes the development of the CFD application and Chapter 6 presents the results of the unsteady odorant transport
simulations that were performed. Finally, Chapter 7 discusses the implications of the results and recommends directions for future work on canine olfaction.

1.2 Literature review

1.2.1 The canine nasal anatomy

The canine nose has three primary physiological functions: conditioning inspired air by moderating temperature and removing particulates, cooling the body through moisture evaporation, and efficiently sensing odorant molecules by way of the large olfactory surface. The nasal cavity is divided into bilaterally-symmetric halves by the nasal septum. Anatomically, each half of the nose is comprised of three main regions: the nasal vestibule, the respiratory region, and the olfactory region. Figure 1.1 shows the anatomy of the canine nasal cavity and Figure 1.2 defines the key anatomical terms of location used herein.

The nasal cavity begins rostrally at the nasal vestibule. The nasal vestibule is responsible for distributing inspired air to the respiratory and olfactory regions of the nose. Due to its sparse vasculature and small surface area, it is unlikely that the nasal vestibule provides significant heat transfer or “air-conditioning” (Negus 1958). Caudally, the nasal vestibule branches into the dorsal and ventral nasal turbinates, the latter of which comprises the maxilloturbinate airway. The maxilloturbinate airway, shown in Figure 1.1, is a fractal-like branching structure that provides a large vascular surface area for heat and moisture exchange. In addition, the maxilloturbinate airway impacts the majority of inspired
Figure 1.1. The canine nasal anatomy. Note that the lamina transversa separates the respiratory and olfactory regions, and the two regions are only connected by the dorsal meatus.
particulate matter before it can reach the lower respiratory tract (Johnston 2002). The maxilloturbinate airway remains separate from the olfactory region and terminates at the nasopharynx which leads to the lower respiratory tract (Evans and Miller 1993).

Figure 1.2. Anatomical terms of location in respect to the canine anatomy.

The dorsal branch of the nasal vestibule becomes the dorsal meatus, a long airway with a tear-drop-like cross-section that runs along the top of the maxilloturbinate airway. The dorsal meatus is only connected to the maxilloturbinate airway by a narrow slit (see Figure 1.1), and otherwise leads directly to the olfactory region, where it terminates. The olfactory region of the nose lies caudal to the respiratory region and is comprised of “scroll-like” ethmoturbinates (Evans and Miller 1993). Olfactory receptor neurons (ORNs), which detect odorant molecules, are located on the ethmoidal surfaces. Ventrally, the
olfactory region joins with the nasopharynx (see Figure 1), providing an outlet for air that enters through the dorsal meatus (Evans and Miller 1993). As emphasized by Craven et al. (2009a), the only pathway of inspired air to the olfactory region during sniffing is via the dorsal meatus.

The frontal sinus is a large empty cavity located dorsal to the olfactory region. It has no respiratory or olfactory function and is connected to the nasal cavity through only the most dorsal of the ethmoturbinates (Evans and Miller 1993).

1.2.1.1 Histology

The canine nasal cavity is lined with epithelium, a membranous tissue comprised of layers of tightly-packed cells. Except for the most rostral portion of the nasal vestibule, the entire nasal cavity is covered with a thin mucus layer having a thickness of approximately 10 μm (Menco 1980). Four primary types of epithelium cover the internal surfaces of the dog’s nose: stratified squamous respiratory epithelium covers the nasal vestibule, pseudostratified respiratory epithelium covers the maxilloturbinate, a thin strip of transitional epithelium provides a histological transition between squamous epithelium and respiratory epithelium, and olfactory epithelium covers the ethmoturbinates (Farmer and Hay 1991). Negus (1958), Nomura et al. (2004), Farmer and Hay (1991), and Anderson et al. (1994) display micrographs of each epithelial type.

Finally, the sinuses are covered with respiratory epithelium, except where the ethmoturbinates and sinuses merge. In this region, olfactory epithelium may be found. Figure
1.1 shows the approximate locations of respiratory (non-sensory) and olfactory (sensory) epithelium in the nasal cavity.

1.2.1.2 Respiratory mucosa

Mucosa is comprised of epithelium and the thin mucus layer that covers it. There is plentiful vasculature beneath the mucosa in regions of the nose covered with respiratory epithelium (Negus 1958). Dilation and constriction of this vasculature is responsible for the nasal cycle, which causes a rhythmic alternation in airflow resistance across the nasal cavity (Bojsen-Moller and Fahrenkrug 1971). Although the nasal cycle has not been observed directly in the dog, it has been documented in other keen-scented (macrosmatic) animals, e.g. carnivores, rodents, and marsupials. Currently, the purpose of the nasal cycle is not well understood.

Secretions from glands interspersed in the respiratory epithelium create a heterogeneous mucus layer, consisting of a low-viscosity watery base layer and a more-viscous gel-like superficial film (Matsui et al. 1998; Schipper et al. 1991). During respiration, evaporation from the respiratory mucus layer humidifies inspired air and provides evaporative cooling (Negus 1958). Motile cilia, which project from the respiratory epithelium, “beat” cyclically in the mucus at approximately 10-20 Hz. Ciliary motion induces a mucus flow from the respiratory airways towards the nasopharynx at approximately 2.5 mm/min (Matsui et al. 1998), where the mucus is eventually swallowed. Functionally, mucus flow provides a mechanism for clearing impacted particulates from the nasal cavity (Schipper et al. 1991).
1.2.1.3 Olfactory mucosa

Figure 1.3 presents a cross-sectional diagram of the olfactory mucosa. As shown, the olfactory epithelium is comprised of ORNs, supporting cells, and basal cells which can mature into ORNs. ORNs are bipolar neurons with a single dendrite that projects to the surface of the olfactory epithelium and a single axon connected to the olfactory bulb. 10-30 olfactory cilia, each having a diameter of 0.2 – 0.3 μm and a length of 50 μm, project from each dendrite (Leinders-Zufall et al. 1998; Menco 1997). In contrast to the motile respiratory cilia, olfactory cilia are intertwined and lay limp, completely covering the surface of the olfactory epithelium beneath the mucus layer (Morrison and Costanzo 1990).

Figure 1.3. A cross-sectional schematic of the mammalian olfactory mucosa. Adapted from Craven (2008).
Microstructurally, olfactory mucus differs from respiratory mucus. Olfactory cilia lie in a viscous gel-like layer which is covered by a superficial watery layer (Getchell et al. 1984, 1993). The composition of the mucus layer is complex, containing numerous proteins, the majority of which have unknown functions (Débat et al. 2007). Of particular note are the olfactory-binding proteins, which appear to aid in odor detection. It has been shown that vertebrate olfactory-binding proteins bind with hydrophobic odorants, possibly aiding the transport of these insoluble odorants through the aqueous mucus layer to olfactory receptor binding sites. (D’Auria et al. 2006). Unfortunately, at the present time, the function of olfactory-binding proteins is still controversial (Pelosi 2001, 1996; Tegoni et al. 2000), making it impossible to properly account for their presence in odorant transport models.

1.2.1.4 Olfactory receptors

Olfactory receptors, which bind odorant molecules, are embedded in the surfaces of the olfactory cilia that emanate from ORNs (see Figure 1.3). The dog has at least 1094 unique olfactory receptor types, of which 20.3% are pseudogene receptors that are non-functional evolutionary relics (Quignon et al. 2003, 2005). For comparison, humans have 862 olfactory receptors types of which 56% are pseudogene receptors (Gilad et al. 2005), explaining some of the observed difference in human and canine olfactory acuity. Each active olfactory receptor recognizes multiple odorants, and the overall olfactory system uses a combinational encoding scheme to recognize thousands of unique smells (Malnic et al. 1999; Buck 2004).
In vertebrates, families of olfactory receptors with similar molecular binding affinities are found in non-overlapping rostro-caudal expression zones. To date, at least four of these zones have been genetically identified in the rat (Ressler et al. 1993; Vassar et al. 1993; Mombaerts et al. 1996) and mouse (Nef et al. 1992). Although olfactory receptor expression zones have not yet been mapped in the dog, we can assume an analog with those in the rat. Figure 1.4 shows the relative location of the different expression zones in the olfactory region of the rat, which has a nasal anatomy that is similar to the dog.

Figure 1.4. Olfactory receptor expression zones in the rat. Each color represents a different expression zone. (Left) A sagittal section of the nasal cavity. (Right) A transverse section of the olfactory region. Adapted from Buck (2005)
1.2.2 The physical phenomena of odorant transport during canine olfaction

Olfaction begins when the dog sniffs, drawing odorant molecules into the nasal cavity with the inspired airflow. Odorant-laden airflow is then delivered to the olfactory region of the nose via a high-velocity (on the order of 10 m/s) airstream through the dorsal meatus (Craven et al. 2009b,a). As odorant-laden airflow slowly filters through the olfactory region, odorant sorption occurs at the air-mucus interface, whereby odorant molecules enter the thin mucus layer that covers the olfactory surfaces. Figure 1.5 illustrates the transport phenomena that occur in the olfactory region.

Figure 1.5. Odorant transport phenomena in the nasal airways and the mucus layer.
In the mucus layer, odorant molecules diffuse through the approximately-stagnant mucus (Moulton 1976) towards the surface of the olfactory epithelium. Odorant molecules that reach the epithelial surface are bound by G-protein-coupled olfactory receptors embedded in the cilia, initiating the transduction cascade which transforms information about odorant molecules into electrical signals that are interpreted by the brain as scents (Firestein 2001; Schild and Restrepo 1998). The perceived strength of a scent is a function of the number of stimulated ORNs and the binding rate of odorant molecules at the epithelial surface.

After a short dwell time (about 1 ms according to Bhandawat et al. (2005)) at the olfactory receptor sites, odorant molecules are cleared or consumed by a biological process, although the exact mechanism by which this occurs remains unclear. Ambiguities associated with the mechanisms of odorant binding and clearance at the ORN sites make it difficult to model the biophysics of olfaction starting from first principles. A few biophysical models of olfaction (e.g. Kaissling and Rospars 2004; Rospars et al. 2000; Dougherty et al. 2005) have successfully reproduced some key features of the olfactory system, however, these models are necessarily ad hoc and a general model of olfactory is lacking at the present time (de Souza and Antunes 2007).
1.2.3 Studies of nasal airflow

1.2.3.1 Experimental

The mammalian nasal cavity is a labyrinth of interconnected airways, as illustrated in 1.1. The complexity and inaccessibility of these airways has thus far precluded \textit{in vivo} measurements of nasal airflow in any macrosmatic mammal. Measurements of overall nasal function, such as aerosol retention within the nasal cavity, noxious gas uptake, and airflow resistance have provided valuable insight into the general physiology of the nose, but have taught us little about the internal airflow patterns. Instead, experimental models are commonly used to study internal nasal airflows. Early flow visualization studies in the human (Hornung et al. 1987), baboon (Patra et al. 1986), monkey (Morgan et al. 1991; Morgan and Monticello 1990), and rat (Morgan et al. 1991; Morgan and Monticello 1990) were performed with nasal models cast directly from cadavers. While cast models are relatively simple to construct, they are often opaque and are constrained to the same size as the actual nasal cavity. This small model size makes detailed measurements of nasal airflows challenging (Doorly et al. 2008).

Recently, Hopkins et al. (2000) developed a procedure to create transparent models of anatomical structures from magnetic resonance imaging (MRI) or computed tomography (CT) scans using rapid prototyping (RP) manufacturing techniques. The procedure they developed involves three primary steps: First, a three-dimensional computer model of the anatomical structure is reconstructed from MRI or CT scans. Next, a water-soluble negative of the computer model is constructed using a RP technique and the negative is
sealed with a water-soluble glue. Finally, the RP negative is cast in silicone polymer and then dissolved with water to reveal the final silicone model.

The optical properties of models constructed using this technique are superior to those of models cast from cadavers. Moreover, large-scale (i.e. any scale greater than 1:1) RP models can be constructed and used to make detailed flow measurements by way of dynamic scaling. Hopkins et al. (2000) constructed a human nasal cavity model with this technique and used it to acquire the first PIV measurements of nasal airflow. Several other studies (reviewed by Chung and Kim (2008)) have since used PIV measurement techniques to study various aspects of the airflow patterns in the human nasal cavity using similar RP models.

Experimental studies of airflow in the nasal cavity of keen-scented macrosmatic mammals (e.g. the dog and rat) have proven more challenging. The macrosmatic nasal cavity is significantly more complex than that of the human, as illustrated in Figure 1.6. Further, the nasal airways have characteristic diameters on the order of 1 mm, making it difficult to study airflow patterns at a high level of detail at a 1:1 scale. The only experimental studies of nasal airflow patterns in macrosmatic mammals to date have been performed using either cadavers (Dawes 1952; Becker and King 1957) or models cast from cadavers (Cheng et al. 1990; Morgan and Monticello 1990; Morgan et al. 1991). These studies report measurements of airflow resistance and roughly describe the global airflow pattern, but detailed descriptions of the internal nasal airflow are lacking.
Figure 1.6. Representative transverse cross-sections through the nasal cavity of the dog (left) and human (right). Note that the cross-section of the dog’s nose is in the ethmoidal region. The human nasal geometry is reproduced with permission from Liu et al. (2009).

Large-scale models, constructed using RP techniques, could be used to investigate macrosomatic nasal airflow at a level of detail not possible using 1:1 scale models. Unfortunately, it is difficult to use the model construction method developed by Hopkins et al. (2000) for this purpose due to the complexity of the macrosomatic nasal geometry. As Figures 1.1 and 1.6 illustrate, coating the internal surfaces of the dog’s nose evenly with the required sealant would be extremely challenging.
Alternatively, nasal models may be constructed directly at any piratical scale using transparent RP materials (de Zélicourt et al. 2005), thus bypassing the complex positive/negative casting procedure. Unfortunately, transparent RP models are not well-suited for PIV measurements because of poor surface finish and non-uniform optical properties across the thin two-dimensional layers of which they are comprised.

Magnetic resonance velocimetry shows promise as a future technique for making non-invasive flow measurements in complex geometries (Canstein et al. 2008; Elkins and Alley 2007). However, at this time it is not a “turn-key” flow measurement method, and is not suitable for measurements of nasal airflow.

1.2.3.2 Computational

To date, CFD has been the most effective tool for studying nasal airflow in macrosmatic animals. Simulations of nasal airflow in the rat (Kimbell et al. 1993, 1997, 2001; Yang et al. 2007a; Zhao et al. 2006) and dog (Craven et al. 2009b,a) have required the use of large and elaborate computational grids to capture the details of the complex nasal airways. Even so, insufficient grid resolution can cause significant error in the solutions (Craven et al. 2009b). Unfortunately few CFD studies report the numerical error associated with the results.

Such simulations are further complicated by the fact that there may be localized regions of turbulence (e.g. in the nasal vestibule), while the vast majority of the nasal airflow remains completely laminar (Cheng et al. 1990; Morgan et al. 1991; Craven et al. 2007). To avoid the difficulty of simultaneously simulating laminar and turbulent airflow regions,
CFD studies of macrosmatic nasal airflow (Kimbell et al. 1993, 1997, 2001; Yang et al. 2007a; Zhao et al. 2006; Craven et al. 2009b) commonly assume that any turbulence is negligible. Consequently, detailed experimental data are required to validate such CFD simulations to determine if they capture all of the important physical phenomena of nasal airflow.

1.2.4 Computational models of odorant transport during olfaction

There are at least four mechanisms that must be considered when modeling odorant transport from the external environment to olfactory receptors in the nose: (1) Transport of odorant-laden airflow from the external environment, through the nasal airways, to the olfactory region of the nose, (2) sorption of odorant molecules into the mucus layer, (3) diffusion of odorant molecules across the mucus layer towards the olfactory epithelium, and (4) binding and clearance of odorant molecules at the epithelial surface. The first two mechanisms can be modeled with modern CFD techniques by numerically solving the Navier-Stokes and species advection-diffusion equations simultaneously. Modeling the last three mechanisms, however, presents a significant challenge, as the dynamics of odor transport in the mucus layer are not well understood.

Hahn et al. (1994) were the first to address all the important aspects of odorant transport in their one-dimensional steady-state model of human olfaction. Keyhani et al. (1997), Zhao et al. (2004; 2006), and Yang et al. (2007b) used similar models to simulate
steady-state odorant deposition in the nasal cavities of the human and the rat. By considering only steady-state odorant transport, the mucus layer was reduced to an air-phase boundary condition that accounted for sorption, diffusion, and consumption of odorants.

While this methodology (Hahn et al. 1994) is appropriate for modeling simplified steady-state odorant transport in the nose, it fails when transients in the mucus layer must be resolved. In macrosmatic vertebrates, the mucus layer thickness is approximately 10 µm (Menco 1980), sniffing frequencies vary between 4-7 Hz (Craven et al. 2009a; Youngentob et al. 1987; Kepecs et al. 2007), and a typical odorant has a diffusion coefficient of, $D_{om} \sim 1 \times 10^{-9} \text{ m}^2/\text{s}$ in the mucus layer. A scale analysis can be used to show that the time constant associated with odorant diffusion through the mucus layer is, $\tau \sim h_m^2 / D_{om} \sim 0.1 \text{ sec}$. This time constant is of the same order as the time duration of a sniff cycle (Craven et al. 2009a). Thus, although nasal airflow patterns in the dog’s nose are quasi-steady (Craven et al. 2009b), transient effects on odorant transport in the mucus layer may be important and must be considered in a thorough model. To date, no studies of odorant transport in an anatomically-correct nasal geometry have considered such temporal effects.

1.2.5 The nose as a pseudo-chromatographic device

Mozell (1964; 1966; 1970) and Moulton (1976) were the first to describe “chromatographic” separation of odorants in the vertebrate nasal cavity, whereby odorant molecules are deposited non-uniformly along mucus-lined nasal airways. Recent experimental and
computational studies have found that deposition patterns are odorant-specific and depend on the nasal flowfield as well as odorant solubility in the mucus layer (Kurtz et al. 2004; Yang et al. 2007b; Zhao et al. 2006). Further, non-uniform odorant deposition influences the spatial response of the olfactory mucosa to an odorant stimulus (Scott et al. 2006; Kent et al. 1996; Mozell et al. 1987), suggesting that odorant deposition patterns play a significant role in odor recognition (Schoenfeld and Cleland 2005).

In macrosmatic mammals, ORNs of the same type are expressed in rostral-caudal patterns that reach out radially from the nasal septum to fill the nasal cavity (Vassar et al. 1993; Ressler et al. 1993; Strotmann et al. 1994; Mombaerts et al. 1996), as shown in Figure 1.4. Thus, the anatomical organization of ORNs in the olfactory epithelium also influences the response of the olfactory mucosa to an odorant stimulus (Mozell et al. 1987). Accordingly, the “composite” olfactory response is determined by both the odorant deposition pattern “imposed” by the chromatographic effect and by the “inherent” ORN expression topography in the nasal cavity (Mozell et al. 1987; Moulton 1976).

Although ORN expression topography has not yet been mapped for the dog, it has been extensively studied in the rat (Nef et al. 1992; Vassar et al. 1993; Miyamichi et al. 2005), which has a similar nasal anatomical structure (Negus 1958) and a comparable number of functional ORN types as the dog (Quignon et al. 2005; Zhang and Firestein 2002). Given the similarities in the nasal anatomy of canines and rats, the remainder of this dissertation will assume that ORN expression topography is similar in both species unless otherwise noted.
ORNs can generally be divided into two classes. Class I ORNs are described as “fish-like” (Zhang and Firestein 2002) and are sensitive to highly-soluble (hydrophilic) odorants that are rapidly absorbed in the mucus layer. Class II ORNs are more sensitive to insoluble (hydrophobic) odorants. In rats, class I ORNs cover approximately 25% of the epithelial surface area and are expressed primarily in and around the dorsal meatus along the nasal septum, whereas class II ORNs are expressed across all olfactory surfaces (Schoenfeld and Cleland 2005; Mezler et al. 2001; Zhang et al. 2004; Schoenfeld and Knott 2004). Physiological measurements (electroolfactogram and voltage-sensitive dye visualization) corroborate this finding and show that odorant solubility and ORN expression patterns modulate the response of the epithelium to an odorant stimulus (Kent et al. 1996, 2003; Kauer and White 2001). Also, recent electroolfactogram measurements show that highly-soluble odorants evoke strong ORN activity along the nasal septum, whereas insoluble odorants produce a more uniform ORN response throughout the nasal cavity (Scott et al. 2006).

1.2.6 Previous research on canine olfaction at Penn State University

The work presented in this dissertation is a continuation of previous research on the fluid dynamics of canine olfaction performed in the Penn State Gas Dynamics Lab and Applied Research Lab (Settles et al. 2003; Settles 2005; Craven et al. 2007; Craven 2008; Craven et al. 2009b,a). A brief summary of this research is given next in order to provide background for the current work.
1.2.6.1 The canine specimen

An anatomically-correct description of the canine nasal geometry is required to perform experimental and computational studies of airflow and odorant transport. The research presented in this dissertation uses an anatomically-correct computer model of the left nasal cavity of a 29.5 kg mixed-breed female Labrador retriever cadaver. The computer model was reconstructed from 726 high-resolution (180 × 180 × 200 μm) MRI scans by Craven et al. (2007). Figure 1.1 presents the three-dimensional computer model and shows representative transverse slices through the nasal vestibule, respiratory region, and olfactory region. For a more comprehensive description of the cadaver specimen and the creation of the computer model the reader is referred to Craven et al. (2007).

1.2.6.2 CFD simulations of canine nasal airflow

Using the computer model of the canine nasal cavity exemplified in Figure 1.1, Craven et al. (2009b) performed CFD simulations of nasal airflow during the sniff cycle. Thorough grid and timestep studies were performed to verify the solution, although at the time no experimental data were available for validation. The computational simulations of steady odorant transport described in Chapter 4 builds upon this airflow solution.

The computational results of Craven et al. (2009b) showed that respiratory and olfactory airflow follow separate paths through the canine nasal cavity. Herein, “respiratory airflow” is defined as airflow that passes only through airways that are covered with respiratory epithelium and “olfactory airflow” is defined as any airflow that enters the airways
covered with olfactory epithelium. Note that the separate locations of the respiratory and olfactory epithelium are shown in Figure 1.1.

Based on the results from their CFD simulations, Craven et al. (2009a) hypothesized that the nasal anatomical structure of macrosmatic animals, who rely on their sense of smell for survival, is optimized for the efficient delivery of odorant molecules to ORNs in the olfactory region of the nose. Craven et al. (2009a) note that the olfactory region in many macrosmatic animals is relegated to a recess in the rear of the nasal cavity (see Negus (1958)) that is bypassed by respiratory airflow. Moreover, the anatomical configuration of the olfactory region (or olfactory recess) in the dog was shown to force unidirectional laminar airflow during inspiration and a quiescent period during expiration. This unique airflow pattern, combined with the large olfactory surface area for odorant absorption was seen by Craven et al. (2009a) to enhance chromatographic separation patterns, possibly aiding odorant discrimination. In contrast, microsmatic mammals (e.g. humans and primates) do not have such an olfactory recess and nasal airflow patterns in these species vary markedly from those in macrosmatic mammals. Thus, differences in nasal anatomy and resultant intranasal airflow patterns between microsmatic and macrosmatic species may lead to dramatically different odorant deposition patterns, which may partially explain differences in their olfactory abilities.

1.3 Objective

It is the objective of this study to acquire a fundamental understanding of the odorant transport phenomena during canine olfaction. First, an experimental investigation of
nasal airflow is performed to validate current and previous CFD simulations. Next, the physics of odorant transport during olfaction is studied using CFD simulations that consider scalar odorant transport in the nasal airways. The results of this work are intended to contribute to the basic scientific understanding of olfaction, and to the design of biomimetic artificial olfaction devices.
Chapter 2

Flow visualization experiments to describe canine nasal airflow

2.1 Materials and methods

This materials and methods section describes the design and fabrication of an anatomically-correct experimental model of the canine nasal cavity. A scaling method to ensure dynamic similarity between flow in the model and airflow in a live dog’s nose is presented. Finally, the experimental measurement techniques for the flow visualization experiments are described.

2.1.1 Creating an anatomically-correct experimental model of the canine nasal cavity

2.1.1.1 Determination of the scale of the experimental model

As illustrated by Figure 1.1, the canine nasal geometry is very complex, with many airways having a characteristic diameter of approximately 1 mm. As discussed earlier, the small dimensions of the nasal airways make it difficult to study nasal airflow using a 1:1 scale model. Because the goal of the present study is to make detailed observations of nasal airflow patterns, a large-scale model was required. Through careful consideration
it was determined that a 4:1 scale model was large enough to allow detailed observations, and still small enough for laboratory-scale experiments. At 4:1 scale, the nasal cavity is 0.54 m long and has an internal volume of 1.56 L.

2.1.1.2 Selection of a RP technique

At their most basic, RP machines “print” thin (less than 100 µm) two-dimensional layers. A fully three-dimensional part is created from successively printing typically thousands of such layers. During the manufacturing process, support material is added in locations where the model is not self supporting. Support material is then manually removed after construction to reveal the final model.

Flow visualization experiments required a transparent experimental model. Two RP techniques were identified, SLA (using Somos 10120 resin) and PolyJet (using FullCure 720 resin), that are capable of manufacturing transparent parts. A test-part consisting of a transverse section of the intricate maxilloturbinate airways was made with each RP technique. Both of these techniques were able to accurately reproduce the test-part, based on visual inspection and caliper measurements. However, the hard SLA support material could not be removed from internal airways, whereas the soft PolyJet support material was easily removed with a water jet. Thus, the PolyJet technique was chosen to construct the experimental model. We found that the SLA test-part was significantly stronger and had better optical transparency than the PolyJet part. Hence, for less complex models, within which support removal is not a challenge, SLA construction techniques should be considered.
2.1.1.3 Experimental model design and fabrication

Magics RP software (Materialise) was used to design a three-dimensional experimental model using the nasal geometry described above to be manufactured using the PolyJet technique. The sides of the experimental model were made flat to minimize the optical distortion of internal airways. A 2.54 cm diameter barbed tube fitting was added at the exit of the nasopharynx so that fluid could easily be pumped through the experimental model.

Initially, we attempted to manufacture the experimental model as a single part. However, after several failed attempts, it became clear that support material could not be removed from “dead-end” airways if the model was manufactured as a single piece. Thus it became necessary to fabricate the model in 11 separate sections. Alignment pins were added between the sections of the model to insure the sections could be accurately aligned. O-rings were also added between the sections to seal the joints in the model against leakage.

The final experimental model was constructed from FullCure 720 resin using an Eden 500 PolyJet machine with a spatial resolution of 42 µm. At 4:1 scale, the geometric uncertainty from manufacturing (42 µm) was approximately 1% of the diameter of the smallest nasal airways. More importantly, the spatial resolution of the PolyJet manufacturing process far exceeds the resolution of the MRI scans used to create the computer model. Accordingly, the majority of the geometric uncertainty in the experimental model is a result of the MRI reconstruction process (see Craven et al. 2007).
After the experimental model sections were fabricated, the external faces were manually polished with wet sandpaper, starting with 22 µm grit and successively decreasing the grit size to 5 µm. Polishing was finished on a polishing wheel using a 1 µm Al₂O₃ polishing compound. The polished and assembled experimental model is shown in Figure 2.1.

Figure 2.1. The 4:1 scale experimental model of the canine nasal cavity.

It was not possible to polish the internal airways of the experimental model, therefore, they retained some surface roughness as a result of the manufacturing process. This was quantified using an optical profiler and was found to be 36 ± 10 µm. Since surface roughness did not significantly change the overall dimensions of the airways (that have characteristic diameters on the order of 1 mm), it is assumed that flow in the model was not affected by the surface roughness. Surface roughness may hasten transition to
turbulence in the nasal vestibule, but this effect is presumably insignificant compared to
the destabilizing effect the branching structure of the nasal airways has on the airflow
(Peacock et al. 1997).

2.2 Experimental methods

2.2.0.4 Flow rate and pressure loss scaling

Craven et al. (2009a) performed a set of experiments on live dogs to determine the range
of physiological nasal airflow rates. To insure that flow through the present experimental
model maintains dynamic similarity to the flow through a live dog’s nose (specifically,
the dog’s nose that was used to create the computer model of the nasal cavity) we prin-
cipally needed to maintain Reynolds number similarity. For dynamic similarity, Reynolds
number scaling requires that,

\[ u_{\text{model}} = u_{\text{dog}} \left( \frac{1}{\alpha} \right) \left( \frac{\nu_{\text{model}}}{\nu_{\text{dog}}} \right) \]  

(2.1)

Here, \( u \) is the velocity at any point in the nose, \( \alpha \) is the scale of the model, and \( \nu \) is the
kinematic viscosity of the fluid flowing through the nose. The subscripts \( \text{model} \) and \( \text{dog} \)
are used to indicate the experimental model and the live dog’s nose, respectively. The
geometry of the dog’s nose is defined, thus, it follows that,

\[ Q_{\text{model}} = Q_{\text{dog}} \alpha \left( \frac{\nu_{\text{model}}}{\nu_{\text{dog}}} \right) \]  

(2.2)
\[ t_{\text{model}} = t_{\text{dog}} \alpha^2 \left( \frac{\nu_{\text{dog}}}{\nu_{\text{model}}} \right) \]  

(2.3)

where \( Q \) is the flow rate through the nose and \( t \) is the time required for the flow in the nose to travel an arbitrary distance.

To determine a method for scaling static pressure drop across the nose we consider the dog’s nose as a simple flow restriction. The pressure loss, \( \Delta P \), across any flow restriction is a function of the loss coefficient, \( C_L \), and the dynamic pressure,

\[ \Delta P = C_L \rho \overline{U}^2 \]  

(2.4)

Here, \( \overline{U} \) is the average velocity through the flow restriction and \( \rho \) is the fluid density. For constant Reynolds number the loss coefficient is independent of scale. Thus, by combining Equations 2.1 and 2.4 it can be shown that,

\[ \Delta P_{\text{model}} = \Delta P_{\text{dog}} \left( \frac{\rho_{\text{model}}}{\rho_{\text{dog}}} \right) \left( \frac{\nu_{\text{model}}}{\nu_{\text{dog}}} \right)^2 \alpha^{-2} \]  

(2.5)

Equation 2.5 relates the pressure loss across the experimental model to the pressure loss across the live dog’s nose.

The target flow rate for all model experiments was determined using the measurements of Craven et al. (2009a) and Equation 2.2. Additionally, all quantitative data presented herein have been scaled from water or air flow in the 4:1 scale model to airflow in the live dog’s nose using Equations 2.1-2.3 and Equation 2.5. This scaling allows our measurements to be compared directly with previous CFD and experimental results.
2.2.0.5 Experimental setup

Figure 2.2 presents the experimental setup. Water was used as the working fluid for all flow visualization experiments and an adjustable flow rate pump was used to drive flow through the experimental model. By altering the direction of the pumped flow, both inspiration and expiration were simulated. A neutrally buoyant dye, consisting of water and food coloring, was injected using a 5 ml syringe as shown in Figure 2.2. The syringe was fixed in place approximately 25 mm from the front of the nostril for all experiments unless otherwise noted. We insured that the dye streak entering the experimental model was laminar. Accordingly, any observed mixing of the dye streak was caused by the internal nasal flow pattern.
Flow visualization experiments were recorded using a Nikon D90 camera at 24 fps. When a higher frame rate was required to capture details in the flow, a Photron SA-1 camera was used to record the experiments at 250 fps. Dye-structures were difficult to distinguish in SA-1 images because the images had low contrast, as exemplified by Figure 2.3A. For this reason, all images recorded with the SA-1 camera were processed to enhance the contrast of the dye. Specifically, an image of the experimental model with no dye present was subtracted from images with dye present. This process reveals the location of the dye as light regions on an otherwise dark background, as shown in Figure 2.3B.

Air was used as the working fluid to measure the pressure drop across the experimental model over the full range of physiological flow rates. For these measurements, the water pump and flow meter were replaced with a blower and airflow meter, respectively. The pressure drop was then measured with a pressure transducer as shown in Figure 2.2.

Flow mixing in the nasal vestibule creates dye eddies, which then advect downstream into the low Reynolds number regions of the nasal cavity. Eddy-velocimetry was used to measure the velocity of these coherent dye-structures in the flow. If the time interval between two sequential flow visualization images is sufficiently small, the shapes of the dye-structures in the flow do not change significantly as they are advected downstream. Figure 2.4 shows an example of two sequential SA-1 camera images of dye-structures in the maxilloturbinate airways, where the motion of coherent dye-structures is visible. The
Figure 2.3.  (A) An image of dye flow visualization in the respiratory airways of the experimental model captured with the SA-1 high-speed video camera. It is difficult to see the dye-structures because the SA-1 image has poor contrast.  (B) The result of processing the SA-1 image in frame A to enhance the contrast of the dye. The dye is visible as the light regions on the otherwise dark background.
displacement of dye-structures between sequential images was quantified using a custom-written image correlation velocimetry code. Once the displacement was measured, the velocity of the dye-structures was easily calculated because the time interval between images was known. Hargather et al. (2010) provide a thorough description of this eddy-velocimetry technique and the image correlation velocimetry code that was used.

Figure 2.4. Two sequential SA-1 camera images of dye flow visualization in the experimental model. The dashed boxes show representative interrogation windows used for eddy-velocimetry measurements. The motion of the dye-structures between frames A and B is clearly visible.
Eddy-velocimetry is typically used to study two-dimensional flows where the velocity does not vary significantly along the optical path of the camera used to image the flow. In the dog’s nose, the flow field is highly three-dimensional. Thus, the observed velocity of dye-structures could vary between zero (for dye-structures along the walls of the nasal airways) and the maximum fluid velocity along the optical path of the camera. It is important to consider this property of the eddy-velocimetry technique when interpreting the results presented in the next section.

Traditional PIV measurements that require laser-sheet illumination were not possible in the present case due to the poor optical quality of the experimental model. The experimental model did not have a constant index of refraction due to non-uniform optical properties between RP layers, as previously discussed. The non-uniform index of refraction caused laser light passing through the model to be diffracted. Therefore, it was not possible to produce a laser light-sheet inside the model of sufficient quality to allow PIV measurements.

2.3 Results

Flow visualization experiments were performed at nasal flow rates of 15%, 50%, and 100% of the peak inspiratory flow rate. For airflow in the nose of a live dog weighing 29.5 kg (the size of the cadaver from which the experimental model was reconstructed), the peak inspiratory flow rate is approximately 0.45 L/s (Craven et al. 2009a). This corresponds to a water flow rate of 0.14 L/s in the present experimental model. Using
the flow visualization images exemplified in Figures 2.3 and 2.4, the velocity of the flow was measured using the eddy-velocimetry technique previously described. In addition, the pressure drop across the nose was measured over the full range of nasal flow rates.

2.3.1 Inspiratory nasal flow patterns

To study the inspiratory flow patterns a laminar dye-streak was injected at the front of the experimental model as shown in Figure 2.5. Once the dye streak entered the nose it was mixed by turbulence and vortex shedding in the nasal vestibule. The majority of the dye was observed to flow ventrally through the respiratory airways towards the exit of the nasal cavity at the nasopharynx, as seen in Figure 2.5. The remainder of the dye passed above the respiratory airways through the dorsal meatus and entered the olfactory region of the nose. This flow pattern was observed to be similar across all nasal flow rates.

Figure 2.5. Dye flow visualization in the respiratory airways during inspiration at 50% of the maximum physiological flow rate. (A) A laminar dye streak being injected at the front of the nose. (B) The resulting flow pattern in the respiratory region of the nose. The dashed lines illustrate the observed flow direction of the dye.
SA-1 camera video recordings were used to study the details of the flow patterns in the respiratory airways. Figure 2.6 shows three sequential images of dye flow in the respiratory region at 15% of the maximum physiological flow rate. Dye entered the nose as a laminar streak and was mixed by vortex shedding and turbulent-like velocity fluctuations in the nasal vestibule. As the flow advected farther downstream into the maxilloturbinate airways it quickly relaminarized as shown in Figure 2.6C and D.

Figure 2.6. SA-1 camera flow visualization images showing the structure of the flow in the respiratory airways at 15% of the maximum physiological flow rate. (A) The experimental model. The white box indicates the field-of-view for the other images in this figure and the dotted lines delineate the edge of the nasal cavity. (B-D) Sequential flow visualization images in the respiratory airways.
To clearly visualize olfactory flow patterns, dye was injected directly into the dorsal meatus as shown in Figure 2.7. Olfactory flow was advected through the dorsal meatus at a high velocity to the rear of the olfactory region (Figure 2.7A). Next, the flow spread vertically, turned 180 degrees, and filtered slowly forward through the ethmoturbinate airways (Figure 2.7B and C). Eventually, after a tortuous flow path through the ethmoturbinates, the flow exited the nasal cavity through the nasopharynx (Figure 2.7D).

Figure 2.7. Olfactory flow patterns on inspiration at 15% of the maximum physiological flow rate. Frames A-D were extracted from D90 camera video recordings at 3, 6, 17, and 40 seconds (equivalent to 0.06, 0.12, 0.33, and 0.77 seconds for airflow in a live dog’s nose) after the initial dye injection. The dashed lines illustrate the general flow direction of the dye in each image.
The highly three-dimensional nature of the flow in the nasal cavity makes it difficult to illustrate the flow patterns using two-dimensional images. Nonetheless, Figure 2.8A is a schematic diagram that was created to illustrate the observed respiratory and olfactory flow paths with respect to the complex three-dimensional nasal geometry. The light-blue lines show the respiratory flow path. The red, dark-blue, and green lines illustrate representative olfactory flow paths, which are discussed in more detail in a later section. For comparison, Figure 2.8B presents similar streamlines created from CFD simulations performed using the same nasal geometry (Craven et al. 2009b). Overall, there is excellent qualitative agreement between the experimental and CFD results.

2.3.1.1 Influence of the nasal flow rate on inspiratory flow patterns

The respiratory and olfactory flow patterns previously described were markedly similar across all flow rates. The only significant change in the nasal flow patterns with changing flow rate occurred in the nasal vestibule. At low flow rates, mixing in the nasal vestibule was caused primarily by vortex shedding as shown in Figure 2.9A. As the flowrate was increased, turbulent mixing became more prominent. At flowrates above 50% of the maximum physiological value, the flow in the nasal vestibule was predominantly turbulent and laminar dye streaks entering the nose were well mixed before they exited the nasal vestibule, as shown in Figure 2.9B. Regardless of the flow rate, the flow was observed to relaminarize in the majority of the maxilloturbinate airways and in all of the ethmoturbinate airways, where Reynolds numbers are on the order of 100. Given the observed nasal flow patterns, the high level of mixing in the nasal vestibule ensures that a portion
Figure 2.8. A qualitative comparison of experimental and CFD results. (A) A schematic diagram showing the different flow paths observed during dye flow visualization experiments. (B) Streamlines extracted from CFD simulations that were performed using the same nasal geometry (Craven et al. 2009b,a).
of any inspired odor signal reaches the olfactory region. This observation has important implications in understanding how the dog’s nose functions, which is further considered in the Discussion section of this chapter.

2.3.1.2 Effect of the dye injection location on the dye flow path during inspiration

The effect of the dye injection location at the nostril on the dye flow path through the nose is shown in Figure 2.10. The dye flow path was not highly sensitive to the injection location because of mixing in the nasal vestibule. Dye injected in regions 2 and 3 (see Figure 2.10) was well mixed in the nasal vestibule and filled nearly all of the downstream nasal airways. Dye injected in region 1 was not as well mixed, and the majority of dye injected at this location followed a ventral path through the maxilloturbinate as shown in Figure 2.10. The dependence of the dye flow path upon the injection location was observed to be similar across all flow rates tested.

2.3.1.3 Velocimetry measurements

Figure 2.11 presents the results of velocimetry measurements along the dorsal meatus and in the maxilloturbinate airway. The transverse sections of the nasal geometry shown in Figure 2.11 illustrate the regions where measurements were made. The small square and larger triangular symbols represent individual velocity measurements and the average of all measurements at the various axial locations, respectively. For comparison, the corresponding average and maximum velocities extracted from CFD simulation performed
Figure 2.9. The effect of the nasal flow rate on flow patterns in the nasal vestibule. The field of view for these images is similar to that shown in Figure 2.6A. (A) The flow pattern at 15% of the maximum physiological flow rate. At this flow rate, dye mixing is primarily due to laminar mixing and vortex shedding, thus coherent dye-structures are visible. (B) The flow pattern at 100% of the maximum physiological flow rate. At this flow rate, the dye is well mixed near the front of the nasal vestibule by turbulence.
Figure 2.10. (A) The computer model of the nostril showing three dye injection locations. (B-D) Dye flow patterns for injection locations 1, 2, and 3, respectively.
using the same nasal geometry (Craven et al. 2009b) are shown as dashed and solid
lines, respectively. In the olfactory region, the primary direction of the dye-flow was not
normal to the camera line-of-sight. Thus, accurate eddy-velocimetry measurements were
not possible in the olfactory region.

In general, at any axial location, velocimetry measurements varied between just above
zero and a value that is in good agreement with the maximum velocities predicted by
CFD simulations (Craven et al. 2009b). This wide range of velocity measurements was
expected because the flow visualization images captured dye-motion across the entire
optical path of the camera, as previously discussed. Although these eddy-velocimetry
measurements are crude compared to typical PIV data, they nonetheless indicate that
previous CFD simulations (Craven et al. 2009b) and the current experimental results are
in good overall quantitative agreement.

2.3.1.4 Airflow residence time in the olfactory region

The slow filtering of olfactory flow through the ethmoturbinates enhances odorant ab-
sorption by the olfactory mucosa where olfactory receptor neurons are located (Schoenfeld
and Cleland 2005; Cui 1995). For this reason, the residence time of airflow in the olfactory
region is of particular importance in the study of olfaction. Olfactory residence times
were determined by manually analyzing the video recordings of dye flow visualization
experiments. Table 2.1 presents the observed range of olfactory residence times in the
experimental model and the equivalent residence times in the nasal cavity of a live dog at
each flow rate considered. The maximum residence time in sniff cycles (i.e. the number of
Figure 2.11. Eddy-velocimetry measurements at several x/L locations along the axis of the dog’s nose at 50% of the maximum physiological flow rate. The x/L coordinate system is defined in Figure 1.1. Measurements were made in the dorsal meatus (top) and the maxilloturbinate airways (bottom). The small square symbols represent individual velocity measurements and the larger triangular symbols represent the average of the velocimetry measurements at the various axial locations. The transverse sections of the nasal geometry illustrate the regions where the velocimetry measurements were made.
sniffs required for dye to be cleared from the olfactory region) is also presented for reference. The minimum time values in Table 2.1 correspond to the time delay between when dye was injected into the flow and the time at which the dye front reached the exit of the nasal cavity (see Figure 2.7). The maximum residence time was determined when dye was no longer visible in the ethmoturbinate airways. The determination of these times was somewhat subjective because the dye was well-dispersed in the olfactory region as Figure 2.7 shows. Thus, the times presented in Table 2.1, especially the maximum times, should be considered approximate. It is worth noting that these measurements indicate that the maximum residence time in the olfactory region of a live dog at peak inspiration (∼1.6 seconds) is significantly longer than the inspiratory period of the sniff cycle (∼0.1 seconds; Craven et al. 2007). Thus, inspired odorant remains in the olfactory region of the nose for several sniff cycles before exiting the nasal cavity.

Generally, olfactory flow that took the ventral flow path (represented by the green streamlines in Figure 2.8) had the shortest residence time in the olfactory region. Residence time increased as the olfactory flow path moved laterally and dorsally. Olfactory flow that took the most dorsal flow path (represented by the red streamlines in Figure 2.8) entered a region of nearly stagnant flow near the frontal sinus and had the longest residence time in the olfactory region.

### 2.3.2 Expiratory nasal flow patterns

On expiration, flow in the olfactory region was observed to be stagnant, in agreement with Craven et al. (2009a). Dye that was injected into the nasopharynx passed directly
Table 2.1. The observed range of dye residence times in the olfactory region of the experimental model for the three nasal flow rates considered. The equivalent airflow rates and residence times for a live dog are also presented.

<table>
<thead>
<tr>
<th>% of the maximum physiological flow rate</th>
<th>Water flow rate in the model (L/s)</th>
<th>Olfactory residence time in the model (s)</th>
<th>Equivalent airflow rate in the dog’s nose (L/s)</th>
<th>Equivalent olfactory residence time in the dog’s nose (s)</th>
<th>Maximum residence time in sniff cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>0.02</td>
<td>22 to 400</td>
<td>0.07</td>
<td>0.4 to 7.7</td>
<td>39</td>
</tr>
<tr>
<td>50</td>
<td>0.07</td>
<td>7.1 to 180</td>
<td>0.23</td>
<td>0.1 to 3.4</td>
<td>18</td>
</tr>
<tr>
<td>100</td>
<td>0.14</td>
<td>4.0 to 85</td>
<td>0.45</td>
<td>0.08 to 1.6</td>
<td>8</td>
</tr>
</tbody>
</table>
through the maxilloturbinate airways and exited the nose through the nasal vestibule. Dye entering the nasal cavity through the nasopharynx was immediately mixed when the flow impacted the branching airways of the maxilloturbinate. Qualitatively, the flow pattern in the maxilloturbinate and the other respiratory airways (see Figures 2.5, 2.6, and 2.8) was similar on inspiration and expiration even though the flow direction was opposite.

2.3.3 Airflow resistance measurements

The pressure loss across the nose was measured over the full range of physiological flow rates. Figure 2.12 presents the results of these measurements and the corresponding results from CFD simulations (Craven et al. 2009b). There is excellent agreement between the CFD and experimental results. Moreover, given that the CFD simulations assumed the nasal airflow was entirely laminar, these results suggest that viscous pressure losses from turbulence in the nasal vestibule have a negligible effect on the overall pressure drop across the nose.

2.4 Discussion

2.4.1 Comparison of experimental results to previous CFD simulations

The current experimental results are in good agreement with CFD simulations performed using the same nasal geometry (Craven et al. 2009b). Dye flow visualization experiments
Figure 2.12. Pressure drop across the experimental model over the full range of physiological flow rates. The pressure measurements were scaled from airflow in the 4:1 scale experimental model to airflow in a live dog’s nose as described in Section 2. The CFD results of Craven et al. (2009b) are shown for comparison. Representative uncertainty bars are shown for both the experimental and CFD data. The uncertainty in the CFD data was estimated using Richardson Extrapolation Analysis (see Craven et al. 2009b).
revealed a complex inspiratory nasal flow pattern, wherein separate respiratory and olfactory flow paths exist. CFD simulations revealed a very similar flow pattern as illustrated by Figure 2.8. Likewise, both flow visualization experiments and CFD simulations demonstrate that all expiratory airflow bypasses the olfactory region, flows directly through the maxilloturbinate airways, and exits the nasal cavity through the nasal vestibule. Quantitative velocity measurements were also in general agreement with CFD simulations as Figure 2.11 shows.

We observed that laminar mixing (at low flow rates), vortex shedding and turbulence mixed the inspired flow visualization dye streaks in the nasal vestibule. Turbulent flow exiting the nasal vestibule on inspiration quickly relaminarized in the narrow maxilloturbinate airways, and thus had little effect on the overall nasal flow pattern. Pressure drop measurements across the experimental model (see Figure 2.12) are in good agreement with the results of CFD simulations, suggesting that increased pressure loss due to turbulence in the nasal vestibule is negligible.

Although the present experiments showed that there is a small region of turbulent airflow in the nasal vestibule, previous CFD simulations of airflow in the dog’s nose (Craven et al. 2009b) assumed laminar airflow everywhere. Even so, the effects of turbulence on the overall nasal flow pattern are small. Thus, the assumption that nasal airflow is entirely laminar appears to be acceptable if the goal of the CFD simulations is to study airflow in the laminar regions of the nose. However, if details of airflow in the nasal vestibule are of particular importance in future work, the effects of turbulence must be considered.
2.5 Summary

An anatomically-correct 4:1 scale model of the dog’s nasal cavity was designed and fabricated using the PolyJet RP method. The experimental model was used to perform qualitative and quantitative experiments to investigate the internal airflow patterns of the dog’s nose. On inspiration, olfactory and respiratory flow were found to take separate paths through the nasal cavity. Respiratory flow entered the nose and followed a ventral path through the maxilloturbinate airways, completely bypassing the olfactory region. Olfactory flow was conveyed to the rear of the olfactory region through a single airway, the dorsal meatus. From there, olfactory flow slowly filtered forward through the scroll-like ethmoturbinate airways towards the exit of the nasal cavity at the nasopharynx. On expiration, flow in the olfactory region was stagnant and all expired flow passed through the maxilloturbinate airways and exited the nose. The majority of the nasal flow was observed to be completely laminar across all flow rates, although, localized regions of turbulence were observed in the nasal vestibule. Nevertheless, turbulence in the nasal vestibule did not affect the overall flow pattern and the experimental results were in good agreement with previous CFD simulations that assumed that airflow through the canine nose was entirely laminar.

These results represent the most detailed experimental description of nasal airflow patterns in a macrosmatic mammal (e.g. the dog and rat) that is available in the literature. Given the popularity of CFD as a tool to study nasal airflow, these results provide much needed experimental validation. In addition, these experiments allowed the opportunity
to study flow phenomena, such as transition to turbulence and relaminarization, that are difficult to investigate with current CFD methods.
Chapter 3

A mathematical model for odorant transport during olfaction

The remainder of this dissertation focuses on computational modeling of scalar odorant transport during canine olfaction. Before computational simulations can be performed however, a mathematical model that describes the physical phenomena of odorant transport is required.

3.1 Governing equations

A mathematical description of odorant transport during olfaction must consider four separate phenomena: (1) advective-diffusive transport of odorant-laden air from the external environment to the olfactory region of the nose, (2) sorption of odorant into the mucus layer in the olfactory region, (3) diffusion of odorant through the mucus layer towards ORNs at the epithelial surface, and (4) consumption and clearance of odorant at the epithelial surface. The subscripts “a” and “m” will be used to denote properties in the nasal airflow and mucus layer, respectively.
3.1.1 Advective-diffusive transport in the nasal airways

Nasal airflow is responsible for transporting odorant molecules from the external environment to the olfactory region of the nose. A dimensional analysis shows that the buoyancy effects caused by the heating and humidification of inspired air (described by the Grashof number, $Gr_a$) are negligible compared to inertial forces (i.e. $Gr_a/Re_a^2 \ll 1$). Thus, airflow through the nasal airways is governed by the incompressible Navier-Stokes equations, presented here in tensor form.

$$\frac{\partial u_i}{\partial x_i} = 0$$

$$\frac{\partial u_i}{\partial t} + u_j \frac{\partial u_i}{\partial x_j} = -\frac{1}{\rho} \frac{\partial P}{\partial x_i} + \nu \frac{\partial^2 u_i}{\partial x_j^2}$$

where $\nu$ and $\rho$ are the kinematic viscosity and density of air flowing through the nasal cavity, respectively.

In the vapor phase, odorants are transported as passive scalars in the nasal airflow, as governed by the advection-diffusion equation.

$$\frac{\partial C_a}{\partial t} + u_i \frac{\partial C_a}{\partial x_i} = D_{oa} \frac{\partial^2 C_a}{\partial x_i^2}$$

Here, $D_{oa}$ is the binary diffusion coefficient of odorant in air, and $C_a$ is the air-phase odorant concentration.

The Péclet number, $Pe_{d_h} = u_a d_h / D_{oa}$, is a non-dimensional parameter that characterizes the competing effects of advective and diffusive scalar transport phenomena. In the
canine nose, $u_a \sim 1 - 10 \text{ m/s}$ is a characteristic velocity, $d_h \sim 0.001 \text{ m}$ is the characteristic airway diameter, and $D_{oa} \sim 1 \times 10^{-5} \text{ m}^2/\text{s}$ is a characteristic diffusion coefficient, resulting in $Pe_a \gg 1$. This indicates that advection is the dominant mechanism by which odorant molecules are transported into the olfactory region. As expected, diffusion alone is far too slow to serve the purpose of olfaction on the scale of the canine nose.

3.1.2 Odorant transport across the air-mucus interface

As odorant-laden air flows through the olfactory region, odorant sorption occurs at the air-mucus interface, whereby odorant molecules enter the mucus layer (henceforth also referred to as the “mucus-phase”). Figure 1.5 presents a schematic illustration of the transport phenomena that occur during this process. Henry’s Law (Equation 3.4) and conservation of mass (Equation 3.5) govern odorant transport across the air-mucus interface (Kotz et al. 2008),

$$C_a |_{x_n=0} = K_p C_m |_{x_n=0}$$  \hspace{1cm} (3.4)

$$D_{oa} \frac{\partial C_a}{\partial x_n} |_{x_n=0} = -D_{om} \frac{\partial C_m}{\partial x_n} |_{x_n=0}$$  \hspace{1cm} (3.5)

where $C_m$ is the mucus-phase odorant concentration, $D_{om}$ is the binary diffusion coefficient of odorant in the mucus, and $K_p$ is the equilibrium partition coefficient, a measure of odorant solubility. $x_n$ is the direction normal to the air-mucus interface, as illustrated in Figure 1.5.
Henry’s Law permits a discontinuous jump in odorant concentration across the air-mucus interface. Many odorants have a partition coefficient smaller than 1, which causes an amplification of the mucus-phase odorant concentration across the air-mucus interface. In other words, these odorants are hydrophilic. At the air-mucus interface, they preferentially accumulate on the mucus side. During steady inspiration, odorant transport through the nasal airways is a function of the airflow field alone, thus the relative difference in partition coefficients among odorants is directly responsible for creating odorant-specific deposition patterns (also referred to as flux patterns) in the olfactory region.

3.1.3 Odorant transport in the mucus layer

Once odorant molecules have passed across the air-mucus interface, they must diffuse through the mucus layer to the epithelial surface (where olfactory cilia are located) before they can be bound by olfactory receptors. Odorant diffusion parallel to the air-mucus interface is negligible because of the thinness of the mucus layer ($H_m \sim 10 \mu m$ (Menco 1980)) relative to the length of the nasal cavity ($L = 0.13 m$). Also, the time required for mucus motion to remove odorant molecules from the olfactory region (on the order of minutes) is significantly longer than the time it takes an odorant molecule to diffuse across the mucus layer ($\sim 0.1 s$ (Craven 2008)). Odorant transport in the mucus layer is therefore presumed to be one-dimensional and normal to the air-mucus interface, as described by the one-dimensional diffusion equation.

$$\frac{\partial C_m}{\partial t} = D_{om} \frac{\partial^2 C_m}{\partial x_i \partial x_i} \quad (3.6)$$
3.2 Boundary conditions

Given the mixed parabolic-elliptic governing equations, a set of boundary conditions and initial conditions is required to complete the mathematical model.

3.2.1 Airflow boundary conditions

Physiologically-realistic boundary conditions for nasal airflow were determined by Craven et al. (2009a) through a unique set of live-animal experiments. Craven et al. (2009a) measured the nasal airflow rate and sniffing frequency of dogs performing olfactory tasks without harming the animals. These measurements were used to set the nasal airflow rate and sniffing frequency boundary conditions for all CFD simulations. Because mucus layer motion is very slow (~2.5 mm/min (Matsui et al. 1998)) in comparison to the airflow velocity (~10 m/s) in the nasal airways, a no-slip boundary condition was used as an approximation at the air-mucus interface.

3.2.2 Odorant transport boundary conditions

Air-phase boundary conditions  The nondimensional odorant concentration entering the nose through the nasal vestibule was set to $C_\alpha = 1$ for all simulations. As discussed in Chapter 2, expired airflow bypasses the olfactory region and exits the nose. Airflow entering the nasal cavity through the nasopharynx during expiration does not enter the olfactory region (as discussed in Chapter 2), and was observed to have little effect on odorant deposition patterns. Thus, for simplicity, a zero-gradient odorant boundary
condition was used for airflow entering the computational domain from the direction of the nasopharynx.

**Boundary conditions at the air-mucus interface of olfactory airways**

Equations 3.4 and 3.5 provide the appropriate boundary conditions to account for odorant sorption across the air-mucus interface. Enforcing these boundary conditions insures that both Henry’s Law and conservation of mass are satisfied.

**Boundary condition at the surface of the olfactory epithelium**

Once odorant molecules reach the epithelial surface, they are bound by G-protein-coupled olfactory receptors embedded in the cilia membranes (Schoenfeld and Cleland 2005). The dwell time of odorant molecules at the receptor site is on the order of 1 ms (Bhandawat et al. 2005). After being bound, odorant molecules are assumed to be quickly consumed, presumably by odorant-degrading enzymes (Pelosi 1996) or odorant-binding proteins (Steinbrecht 1998; Briand et al. 2002).

The time required for odorant molecules to diffuse through the mucus layer is on the order of 0.1 s (Craven 2008), much longer than the dwell time at the olfactory receptor sites. Consequently, from the perspective of a diffusing molecule, odorants are instantaneously bound and consumed by olfactory receptors as they reach the epithelial surface. Thus, if the olfactory receptors do not become saturated with odorant molecules, the effective odorant concentration at the epithelial surface is taken to be zero (Truskey et al. 2008). This scenario, known as diffusion-limited binding, is physiologically realistic in the case of weak odor signals, where the rate of odorant binding and clearance is much faster.
than the rate of odorant diffusion through the mucus layer towards the epithelial surface. Here, we accept diffusion-limited binding as an appropriate boundary condition.

**Boundary conditions at the air-mucus interface of respiratory airways** As the present study is concerned with odorant transport related to olfaction, the odorant deposition along the respiratory airways that bypass the olfactory region is irrelevant and is not considered. During steady simulations, the linear nature of the advection-diffusion equation that governs odorant transport in the nasal airways allows odorant deposition along the dorsal meatus to be neglected without affecting the odorant deposition patterns in the olfactory region. This is demonstrated computationally in the next chapter. Thus, a zero-odorant-flux boundary condition was specified on all the respiratory surfaces in the nose for simulations of steady odorant transport, including both the maxilloturbinate and the dorsal meatus. Only the olfactory epithelium is allowed to absorb odorant in this model.

A zero-odorant-flux boundary condition is also used for unsteady simulations as a simplifying assumption. A review of the literature reveals that the permeability of the respiratory epithelium is unknown at present, thus it is not possible to formulate a physiologically realistic boundary condition for this surface. Nevertheless, there are no ORNs located in the respiratory epithelium (Buck and Axel 1991), and the rate of diffusion through the respiratory epithelium is assumed to be a slow process on the timescale of a sniff. Thus the zero-odorant-flux assumption is not expected to significantly affect the
results of unsteady simulations. Furthermore, experimentally determining the permeability of the olfactory epithelium is beyond the scope of this research and is left as a topic for future work.

### 3.3 Selection of odorants

Along with nasal airflow patterns, odorant solubility (described by $K_p$) is a primary factor in determining odorant deposition patterns in the olfactory region. It is therefore important to consider odorants with a wide range of $K_p$ values. The three odorants considered here (see Table 3.1) have $K_p$ values that span six orders of magnitude, ranging from insoluble limonene to highly-soluble 2,4-DNT.

Air-mucus $K_p$ values have apparently never been directly measured. Further, analytical methods for determining solubility (Kamlet et al. 1986, 1983) do not account for the complex composition of the mucus layer and cannot be reliably used to estimate air-mucus $K_p$ values. Faced with no other option, it is necessary at present to approximate air-mucus $K_p$ values using the air-water equivalent values, as is common in studies of olfaction (e.g Hahn et al. 1994; Yang et al. 2007b; Zhao et al. 2006; Craven 2008). In line with this, it is appropriate to consider the odorants presented in Table 3.1 as generic odorants that represent highly-soluble, moderately-soluble, and insoluble odorants.
**Table 3.1.** Chemical properties of the odorants presently considered. Partition coefficients were determined using air-water Henry’s Law constants estimated using HENRY-WIN version 3.20 (US Environmental Protection Agency, Estimation Program Interface Suite, http://www.epa.gov/oppt/exposure/pubs/episuite.htm).

<table>
<thead>
<tr>
<th>Odorant</th>
<th>Molecular formula</th>
<th>$K_p$</th>
<th>$D_{oa}$ (m$^2$/s)</th>
<th>$D_{om}$ (m$^2$/s)</th>
<th>$\theta$</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limonene</td>
<td>C$<em>{10}$H$</em>{16}$</td>
<td>1.05</td>
<td>6.30E-06</td>
<td>7.00E-10</td>
<td>1.06E+01</td>
<td>Low</td>
</tr>
<tr>
<td>n-Amyl acetate</td>
<td>C$<em>7$H$</em>{14}$O$_2$</td>
<td>1.59E-02</td>
<td>6.70E-06</td>
<td>7.80E-10</td>
<td>7.32E+02</td>
<td>Moderate</td>
</tr>
<tr>
<td>2,4-Dinitrotoluene (DNT)</td>
<td>C$_7$H$_6$N$_2$O$_4$</td>
<td>2.21E-06</td>
<td>6.50E-06</td>
<td>7.30E-10</td>
<td>5.08E+06</td>
<td>High</td>
</tr>
</tbody>
</table>


### 3.4 Dimensional analysis

Given the complex nature of the odorant transport phenomena, it is useful to perform a dimensional analysis of the problem to gain physical insight. Here, the Buckingham Pi theorem is used to extract the important nondimensional groups for the odorant transport problem.

The first step in dimensional analysis is to identify the variables that parametrize the problem. The variables relevant to the current problem were identified by considering the governing equations developed in Section 3.1. These variables, along with descriptions of their physical significance, are presented in Table 3.2.

In canine olfaction, the dependent variable is the odorant concentration field in the nasal airways and in the mucus layer, $C$. Thus, the functional relationship for the odorant transport problem is defined as,

$$ C = f(C_{inlet}, \omega, U_{inlet-peak}, d_h, L_{olf}, \nu, D_{oa}, D_{om}, \beta) $$  \hspace{1cm} (3.7)

The Buckingham Pi theorem states that the number of unique nondimensional groups that describe a problem is equal to the number of physical variables, minus the minimum number of reference dimensions (Munson et al. 1998). For the current problem, there are three reference dimensions (concentration, length, and time) and eleven physical variables. Thus, choosing the “repeating variables” defined in Table 3.2, the nine nondimensional groups presented in Table 3.3 are derived. Table 3.3 also describes the
physical significance of each nondimensional group and provides order-of-magnitude estimates. Finally, given the relevant set of nondimensional variables, Equation 3.8 describes the nondimensional functional relationship for the odorant transport problem.

\[ C^* = f(Re, \gamma_{olf}, Wo, Sc, \tau_{olf}, h_m^*, \beta) \]  

(3.8)

Given the nondimensional odorant concentration field \( C^* \), the nondimensional odorant flux at the epithelial surface \( J^* \) is easily calculated. At any point along the epithelial surface \( J^* \) has units of \( 1/m^2 \cdot s \). Accordingly, the integral of \( J^* \) across the epithelial surface has units of \( 1/s \). Note that henceforth, only nondimensional odorant concentrations and fluxes will be considered, thus the * indicating nondimensionality will be dropped in both cases.
Table 3.2. Fundamental physical variables of odorant transport during canine olfaction.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Symbol</th>
<th>Units</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odorant concentration at any point in the domain</td>
<td>$C$</td>
<td>mol/m$^3$</td>
<td>Dependent variable</td>
</tr>
<tr>
<td>Inlet airflow odorant concentration</td>
<td>$C_{inlet}$</td>
<td>mol/m$^3$</td>
<td>Repeating variable</td>
</tr>
<tr>
<td>Sniff frequency</td>
<td>$\omega$</td>
<td>s$^{-1}$</td>
<td>Repeating variable</td>
</tr>
<tr>
<td>Mean inlet velocity at peak inspiration</td>
<td>$U_{inlet-peak}$</td>
<td>m/s</td>
<td>Repeating variable</td>
</tr>
<tr>
<td>Airway hydraulic diameter</td>
<td>$d_h$</td>
<td>m</td>
<td>Airway length scale</td>
</tr>
<tr>
<td>Length of olfactory region</td>
<td>$L_{olf}$</td>
<td>m</td>
<td>Airway length scale</td>
</tr>
<tr>
<td>Kinematic viscosity of air</td>
<td>$\nu$</td>
<td>m$^2$/s</td>
<td>Air-phase fluid property</td>
</tr>
<tr>
<td>Binary diffusion coefficient of odorant in air</td>
<td>$D_{oa}$</td>
<td>m$^2$/s</td>
<td>Air-phase fluid property</td>
</tr>
<tr>
<td>Binary diffusion coefficient of odorant in mucus</td>
<td>$D_{om}$</td>
<td>m$^2$/s</td>
<td>Mucus-phase fluid property</td>
</tr>
<tr>
<td>Mucus thickness</td>
<td>$h_m$</td>
<td>m</td>
<td>Mucus-parse length scale</td>
</tr>
<tr>
<td>Equilibrium partition coefficient</td>
<td>$\beta$</td>
<td>-</td>
<td>Air-mucus interface property</td>
</tr>
</tbody>
</table>
Table 3.3. Nondimensional parameters governing odorant transport in the canine nasal cavity.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Symbol</th>
<th>Definition</th>
<th>Order of magnitude estimate</th>
<th>Physical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondimensional odorant concentration</td>
<td>$C^*$</td>
<td>$C/C_{inlet}$</td>
<td>1</td>
<td>Ratio of odorant concentration to the inlet concentration</td>
</tr>
<tr>
<td>Reynolds number</td>
<td>$Re_{d_h}$</td>
<td>$\frac{U_{inlet-peak} d_h}{\nu}$</td>
<td>100-1000</td>
<td>Ratio of inertial to viscous effects</td>
</tr>
<tr>
<td>Nondimensional olfactory time scale</td>
<td>$\gamma_{olf}$</td>
<td>$\frac{\omega L_{olf}}{U_{inlet-peak}}$</td>
<td>0.1</td>
<td>Ratio of advective to diffusive mass transport time in the air-phase</td>
</tr>
<tr>
<td>Womersley number</td>
<td>$Wo_{d_h}$</td>
<td>$\frac{d_h}{\frac{\omega}{\nu}}$</td>
<td>1-10</td>
<td>Characterizes the nature of unsteady flow</td>
</tr>
<tr>
<td>Schmidt number</td>
<td>$Sc$</td>
<td>$\frac{\nu}{\nu_{pa}}$</td>
<td>&gt;1</td>
<td>Ratio of viscous to mass diffusivity in the air-phase</td>
</tr>
<tr>
<td>Normalized time scale</td>
<td>$\tau_{olf}$</td>
<td>$\frac{h_{\omega}^{2} \omega}{D_{om}}$</td>
<td>0.01</td>
<td>Ratio of mucus diffusive time scale to sniff time scale</td>
</tr>
<tr>
<td>Normalized mucus height</td>
<td>$h_{m}^*$</td>
<td>$\frac{h_{m}}{d_{h}}$</td>
<td>0.01</td>
<td>Ratio of the airway diameter to the mucus layer height</td>
</tr>
<tr>
<td>Partition coefficient</td>
<td>$\beta$</td>
<td>$\frac{C_{ia}^<em>}{C_{im}^</em>}$</td>
<td>$1 \times 10^{-6} - 1$</td>
<td>Odorant solubility</td>
</tr>
</tbody>
</table>
Chapter 4

Simulating odorant transport
during steady inspiration

4.1 Materials and methods

4.1.1 Generation of an anatomically-correct computational mesh

The complexity of the canine nasal airway precluded the use of structured computational meshing techniques. Instead, a semi-automated octree-based method (Harpoon, Sharc Ltd.) was used to generate a 104-million-element hexahedral-dominant mesh that also contained wedge, pyramid, and tetrahedral elements (Craven et al. 2009b). Figure 4.1 shows the computational domain, including illustrations of the mesh resolution achieved in the respiratory and olfactory airways.

4.1.2 Airflow solution

Craven et al. (2009b) performed high-fidelity steady state computational fluid dynamics simulations of canine nasal airflow using the computer model of the canine nasal anatomy presented in Figure 1.1. Craven et al. (2009b) provide a thorough discussion of the numerical methods and boundary conditions that were used, thus, only a brief overview is given here.
Figure 4.1. The computational domain. The mesh resolution in the respiratory (left) and olfactory (right) regions of the nasal cavity are shown.
The majority of the canine nasal airflow has a Reynolds number on the order of 100 (Craven et al. 2007, 2009b). Thus, turbulence was not considered in the airflow simulations. Additionally, buoyancy effects caused by the heating and humidification of inspired air are negligible compared to inertial and viscous effects and were not considered. Under this set of assumptions, the steady incompressible Navier-Stokes equations govern airflow through the nose and were solved over the computational mesh using the commercial computational fluid dynamics (CFD) code Acusolve (ACUSIM Software Inc.). Physiologically-realistic nasal airflow rates, determined through a set of live-animal experiments (Craven et al. 2009a), were used as boundary conditions for the airflow simulations. The nasal airways were given a no-slip boundary condition and a zero-gradient velocity condition was prescribed on the edges of the computational domain shown in Figure 4.1. A pressure differential was specified across the nose to drive the airflow for all simulations.

4.1.3 Numerical solution of the mathematical model of odorant transport during canine olfaction

Given the previously verified airflow solutions (Craven et al. 2009b), the commercial CFD software package Acusolve (ACUSIM Software Inc., see Shakib (1989) and Hughes et al. (1986)) was used to solve Equation 3.3 for odorant transport over the computational mesh of the canine nasal cavity. Simulations were performed with each odorant listed in Table 3.1 for nasal airflow rates 2.5% (0.05 L/s), 25% (0.22 L/s), and 100% (0.46 L/s) of the maximum inspiratory value. The nondimensional odorant concentration entering the
nose was set to $C_a = 1$ for all simulations. Since expiratory airflow completely bypasses the olfactory recess during sniffing (see Craven et al. (2009a), Figure 5c), this phase of a sniff has no effect on odorant transport patterns in the olfactory recess and was therefore not considered in the present study. The odorant transport phenomena in the mucus layer covering the nasal cavity were simulated using the air-phase boundary conditions described in the following two sections.

4.1.4 Odorant transport boundary condition on olfactory airways

In general, odorant transport in the air and mucus phases must be simulated simultaneously using Equations 3.4 and 3.5 to couple the solutions across the air-mucus interface. To simplify the solution procedure for steady state simulations, mucus layer transport was reduced to an air-phase boundary condition using a method first demonstrated by Keyhani et al. (1995). At steady-state, according to the present assumptions, the odorant concentration profile is linear across the mucus layer with a concentration of zero at the epithelial surface. Combining this linear profile with Equations 3.4 and 3.5 results in Equation 4.1, an air-phase boundary condition that accounts for odorant sorption, diffusion, and consumption in the mucus layer. Equation 4.1 was applied as a boundary condition on all olfactory surfaces in the nose (see Figure 1.1).

$$\frac{\partial C_a}{\partial x_n} |_{x_n=0} + \theta C_a |_{x_n=0} = 0$$  \hspace{1cm} (4.1)

$$\theta = \frac{D_{om}}{D_{oa} h_m K_p}$$  \hspace{1cm} (4.2)
The nondimensional parameter $\theta$ describes how readily odorant molecules are transported from the airstream to the epithelial surface. Thus, along with the nasal airflow patterns, $\theta$ values determine odorant transport patterns in the nasal cavity during steady inspiration. For $\theta \gg 1$, Equation 4.1 approaches a zero-concentration boundary condition, representing a highly-soluble odorant that is instantly transported through the mucus layer and consumed at the epithelial surface. Conversely, for $\theta \to 0$, Equation 4.1 becomes a zero-odorant-flux boundary condition, representing an odorant that is not absorbed into the mucus layer at all.

The odorant diffusion coefficients, $D_{om}$ and $D_{oa}$, are similar for most odorants (see Table 3.1), and the mucus layer thickness, $h_m = 10 \mu m$ (Menco 1980), is not expected to vary by more than a single order-of-magnitude. Accordingly, the value of the $\theta$ parameter is influenced primarily by the air-mucus partition coefficient, $K_p$, which spans six orders-of-magnitude for the odorants considered. Thus, while variations in the mucus layer thickness will slightly affect odorant transport patterns, the effect is presumably insignificant because variations in $K_p$ dominate changes in $\theta$ values.

4.1.5 Odorant transport boundary condition on respiratory airways

Previous CFD simulations (see the Results section in this chapter and Craven et al. 2009b) have shown that only the mucus-coated dorsal meatus delivers airflow to the olfactory region of the dog’s nose. Airflow through all other respiratory airways completely bypasses the olfactory region (Craven et al. 2009b), thus odorant deposition in these
airways is irrelevant to olfaction (although certainly still relevant in toxicology and other concerns beyond the present scope).

As the present study is focused on odorant transport as it related to olfaction, it is not necessary to simulate deposition in the respiratory airways that bypass the olfactory region. Further, because the advection-diffusion equation (Equation 3.3) that describes odorant transport in the nasal airways is linear, odorant deposition along the dorsal meatus does not significantly affect the normalized odorant transport patterns in the olfactory region. To demonstrate, consider the two scenarios described below in which odorant deposition in the olfactory region is modeled and the odorant concentration entering the nose is $C_a = 1$.

- **Scenario A:** No odorant is deposited along the dorsal meatus and a zero-odorant-flux boundary condition is prescribed on its surface. The airflow odorant concentration profile entering the olfactory region through the dorsal meatus is therefore uniform with a value of $C_a = 1$.

- **Scenario B:** Odorant absorption in the mucus layer covering the dorsal meatus is modeled, whereby odorant molecules are deposited and consumed. The airflow odorant concentration entering the olfactory region is therefore less than the concentration at the inlet of the nasal cavity. Further, the odorant concentration profile in the dorsal meatus is non-uniform due to concentration boundary layers that form along it.
Clearly, the amount of odorant deposited in the olfactory region will be less in Scenario B than in A. However, because of the linear nature of Equation 3.3, it is valid to scale the odorant concentration in the nasal cavity by a constant value without altering the physics of the problem. This allows the assumption that deposition along the dorsal meatus is negligible. For example, assume that in Scenario B 50% of the inspired odorant is absorbed along the dorsal meatus, yielding a mass-averaged odorant concentration of $C_a = 0.5$ entering the olfactory region. If the odorant concentration is now scaled by a factor of two, $C_a = 2$ entering the dog’s nose and the mass-averaged value $C_a = 1$ entering the olfactory region is restored. Linear scalability thus makes Scenarios A and B equivalent for normalized odorant transport patterning in olfactory region, and renders the degree of odorant deposition along the dorsal meatus irrelevant during steady inspiration.

Two preliminary CFD simulations were performed to test the above conclusion. Scenario A was modeled in the first, wherein a zero-odorant-flux boundary condition was prescribed along the dorsal meatus. In this case no odorant deposition occurred prior to the olfactory region. In the second simulation Scenario B was modeled, wherein Equation 4.1 was used as a boundary condition along the dorsal meatus to simulate diffusion-limited odorant absorption.

Figure 4.2 presents the resulting odorant concentration profiles in a representative transverse cross-section of the olfactory region for Scenarios A and B, for the odorants DNT (highly-soluble) and limonene (essentially insoluble). The odorant concentration in Scenario B was scaled, as described above, so that the mass-averaged odorant concentration
entering the olfactory region remained approximately $C_a = 1$, the same value as in Scenario A. Figure 4.2 reveals almost-identical odorant concentration profiles for both scenarios under these conditions, regardless of whether the odorant in question was highly-soluble or insoluble. This analysis demonstrates two things: (1) the effect of odorant absorption by the respiratory mucus preceding the olfactory region can be accounted for during steady inspiration by properly scaling the odorant concentration, and (2) odorant absorption along the dorsal meatus can be neglected without affecting the normalized odorant deposition patterns in the olfactory region. As already stated, odorant absorption in all respiratory airways other than the dorsal meatus is also negligible for present purposes, since those airways have been demonstrated to entirely bypass the olfactory region.

Therefore, in order to simplify the present CFD simulations, odorant deposition in the mucus layer that covers the dorsal meatus and all other respiratory airways was not simulated. Instead, these airways were given a zero-odorant-flux boundary condition,

$$\frac{\partial C_a}{\partial x_n} |_{x_n=0} = 0$$

(4.3)

The results of the preliminary CFD simulations and the above argument show that this simplification is reasonable, and has a negligible effect upon normalized odorant deposition patterns in the olfactory region during steady inspiration.
Figure 4.2. A comparison of odorant concentration profiles of DNT and limonene in a representative transverse cross-section of the olfactory region for deposition Scenarios A and B. The color scales represent the normalized odorant concentration in the nasal airways. Note that the arrows show regions where the concentration profiles were noticeably different. The concentration of DNT in Scenario B was scaled by a factor of 1.9 to account for odorant loss in the dorsal meatus. The concentration of limonene in Scenario B was not scaled because the required scaling factor was approximately 1.
4.2 Results

4.2.1 Nasal airflow patterns

The canine nose is responsible for both respiratory and olfactory functions. As these two functions have unrelated objectives, it is not surprising that the nose has evolved separate flowpaths for each (Craven et al. 2009a). Figure 4.3 shows several inspiratory streamlines that reveal the existence of separate olfactory and respiratory airflow paths through the nasal cavity. Respiratory airflow exits the nasal vestibule and flows ventrally through the maxilloturbinate airway towards the nasopharynx, where it enters the lower respiratory tract, completely bypassing the olfactory recess.

The olfactory flowpath is significantly more complex: a single airway (the dorsal meatus) transports odorant-laden airflow around the maxilloturbinate airway directly to the rear of the olfactory recess (see Figure 4.3). From there the flow turns 180 degrees and filters slowly forward through the more peripheral olfactory “scroll-work” towards the nasopharynx. The most significant distinction between the various olfactory streamlines is their residence time in the olfactory recess. In general, olfactory airflow that passes through the dorsal ethmoturbinates resides in the nasal cavity significantly longer than olfactory flow that passes through the ventral or lateral ethmoturbinate regions. Across all flow rates, olfactory airflow comprises approximately 15% of the total airflow inspired by the dog, the remainder going towards respiration. The flow patterns described above and shown in Figure 4.3 do not vary significantly as a function of the inspired airflow rate.
Present simulations show that nasal airflow patterns in the dog are similar to those previously reported for the rat (Morgan et al. 1991; Zhao et al. 2006; Yang et al. 2007a; Kimbell et al. 1997). Specifically, the dog’s nasal flowfield has an s-shaped olfactory flowpath similar to the flowpath in the rat (the green streamline in Figure 4.3). In addition, the dog has a set of dorsal ethmoidal scroll-work that is not present in the rat. This additional set of olfactory scroll-work provides a dorsal olfactory flowpath (the red streamline in Figure 4.3) that has not been observed in the rat. A more thorough discussion of canine nasal airflow patterns is provided by Craven et al. (2009a).

4.2.2 Epithelium flux patterns in the canine olfactory recess

During steady inspiration, odorant flux to the olfactory epithelium determines the strength of an odor signal delivered to the ORNs. Figure 4.4 shows surface contours of odorant flux to the olfactory epithelium on the external surfaces of the nasal cavity. Note that the contour legends in Figure 4.4 vary over four orders of magnitude for the different odorants.

While the surface contours of Figure 4.4 illustrate the epithelial flux patterns on external surfaces of the olfactory recess, the internal scroll-like surfaces remain obscured. Transverse sections of airstream concentration, presented in Figure 4.5, are the most effective method of visualizing odorant transport patterns in these internal airways. Figure 4.5 shows the nondimensional odorant concentration profiles for the three odorants considered at each flow rate simulated. Note that the surface concentration shown in Figure 4.5 is directly related to surface flux as described by Equation 4.1.
Figure 4.3. Inspiratory airflow patterns in the canine nasal cavity at peak inspiration (0.46 L/s). Airflow enters the nose at the left through the nasal vestibule. The red, dark blue, and green streamlines illustrate the dorsal, lateral, and ventral olfactory flowpaths, respectively. The arrow heads on the olfactory streamlines represent the direction of the airflow. The orientation of the nasal cavity is similar to that shown in Figure 1.1.
DNT, which is highly-soluble, is quickly absorbed upon entering the olfactory recess, resulting in the high odorant fluxes observed along the dorsal meatus and nasal septum (see Figures 4.4a and 4.5a-c). The olfactory airstream is nearly depleted of DNT before the airflow reaches the rear of the olfactory recess and begins filtering forward.

Amyl acetate is moderately-soluble in the mucus layer, so its flux patterns are found to be highly dependent upon the olfactory flowpath (see Figures 4.4b and 4.5d-f). Airflow that takes the short ventral path through the olfactory recess is not significantly depleted of amyl acetate. In contrast, airflow taking the longer dorsal path is almost completely depleted of amyl acetate upon exiting the nasal cavity through the nasopharynx. The non-uniform absorption patterns for amyl acetate cause highly non-uniform odorant flux across the olfactory epithelium at all airflow rates.

Lastly, limonene is weakly absorbed by the mucus layer and the entire olfactory recess is exposed to nearly-uniform limonene concentration, except at the lowest flowrate, at which there is significant limonene absorption along the dorsal meatus and nasal septum (see Figures 4.4c and 4.5g-i). Furthermore, as shown in Figure 4.4, limonene surface fluxes are low in relation to the other odorants considered due to limonene's large partition coefficient.

4.2.3 The effect of airflow rate on epithelium flux patterns

Nasal airflow rate also affects the epithelium flux patterns as illustrated in Figure 4.5. At low flow rates, the dorsal meatus absorbs the majority of odorant before it reaches the more peripheral olfactory scroll-work. With increasing airflow rate, odorant-laden
Figure 4.4. Surface contours of odorant flux to ORNs in the olfactory recess in units of $1/m^2\cdot s$ (see Chapter 3) for (a) DNT, (b) amyl acetate, and (c) limonene at peak inspiration (0.46 L/s). The left and right views in each panel show the olfactory recess viewed from lateral and medial perspectives, respectively. Non-olfactory surfaces are colored gray. As shown, the flux to ORNs is non-uniform for (a) DNT and (b) amyl acetate, but it is roughly uniform for (c) limonene. Note that the contour legends vary over four orders of magnitude for the different odorants.
Figure 4.5. Transverse contours of nondimensional odorant concentration in the olfactory recess for: (a-c) DNT, (d-f) amyl acetate, and (g-i) limonene. Airflow rates of (a,d,g) 0.05 L/s, (b,e,h) 0.22 L/s, and (c,f,i) 0.46 L/s are shown for each odorant. Note that the left-most transverse slice in each panel contains some non-olfactory airways (see Figure 1.1). Although the concentration in these non-olfactory airways is 1, there is no odorant flux to these surfaces.
air is advected farther into the olfactory scroll-work before the odorant becomes depleted from the airstream. In effect, increasing the nasal flow rate causes odorant molecules to be deposited across a larger percentage of the dog’s olfactory surface area, while simultaneously increasing odorant surface flux. As shown in Figures 4.4 and 4.5, nasal flow rate has a large effect on flux patterns of amyl acetate (moderately-soluble) and limonene (insoluble), but has limited effect on the flux patterns of DNT (highly-soluble). Physically, this is because DNT is almost completely absorbed before it reaches peripheral olfactory scroll-work, where variations in flux patterns with changing flow rate are most apparent.

To quantify the effect of partition coefficient and flow rate on epithelial flux in the nasal cavity we define a normalized odorant removal efficiency of the olfactory recess as:

\[ \eta = 1 - \frac{J_{\text{out}}}{J_{\text{in}}} \]  

(4.4)

\( J_{\text{in}} \) and \( J_{\text{out}} \) are the airborne odorant fluxes into and out of the olfactory recess, respectively. A removal efficiency of 1 indicates that the odorant was completely absorbed in the olfactory recess. Figure 4.6 presents a plot of the removal efficiency for each odorant considered here as a function of the nasal airflow rate. The odorant removal efficiency is observed to increase rapidly with decreasing odorant partition coefficient. At peak inspiration, the removal efficiency increases from 4% for limonene to 81% for DNT. Increasing the airflow rate has the effect of decreasing the removal efficiency for all odorants.
This trend is somewhat misleading, however, since the total odorant uptake of the olfactory recess increases significantly with airflow rate as illustrated by Figure 4.7. Thus, “sniffing harder” to increase nasal airflow rate decreases the removal efficiency of the olfactory recess, but nonetheless provides a larger odorant flux to the ORNs. Behavioral evidence suggests that macrosmatic mammals may take advantage of this phenomenon by increasing their inspiratory flow rate to maximize odorant uptake when trying to detect low-concentration odors (Youngentob et al. 1987). This principle is also important to bio-inspired “mechanical sniffer” designs for use in chemical trace detection applications (Settles 2005).

4.2.4 Comparison of the present results with epithelial flux patterns in the nasal cavity of the rat

For insoluble odorants, the present simulations predict significantly-different epithelial flux patterns than similar computational studies in the rat have reported (Zhao et al. 2006; Yang et al. 2007b). Yang et al. (2007b) found that insoluble odorants are deposited primarily on peripheral scroll-like olfactory surfaces. Whereas, as previously discussed, our results show that insoluble odorants are absorbed almost uniformly over all olfactory surfaces for airflow rates between 25% and 100% of the maximum inspiratory airflow rate. At very low nasal airflow rates (5% of the maximum value, see Figure 4.5g), we observe patterns opposite those reported by Yang et al. (2007b). Specifically, at low flow rates all of the odorants, including insoluble limonene, are absorbed appreciably in the dorsal meatus before the olfactory airflow turns 180 degrees and filters back through
Figure 4.6. Normalized odorant removal efficiency (Equation 4.4) of the olfactory recess as a function of nasal airflow rate.
Figure 4.7. Total odorant uptake by the olfactory recess as a function of nasal airflow rate.
the olfactory scroll-work. Hence, at low nasal flow rates we observed odorant flux to be higher along medial olfactory surfaces around the dorsal meatus than in the more peripheral olfactory scroll-work.

4.3 Discussion

4.3.1 Correlation between epithelial odorant flux patterns and ORN expression topography

Our results indicate that soluble and insoluble odorants are transported to the ORNs by different mechanisms. Highly-soluble odorants, such as DNT, are deposited mainly along the dorsal meatus and nasal septum near the entrance to the olfactory recess (see Figure 4.5) where class I ORNs that are sensitive to highly-soluble odorants are expressed. Moreover, because odorant-laden air is delivered to the olfactory recess via a high-velocity airstream in the dorsal meatus, odorant absorption on non-olfactory surfaces is minimized. Since the canine olfactory recess is located at the rear of the nasal cavity, this rapid transport mechanism appears to permit the detection of highly-soluble odorants that would otherwise be absorbed prior to reaching the olfactory recess.

The mechanism through which moderately-soluble and insoluble odorants are transported to ORNs is significantly different. Amyl acetate and limonene fluxes to the olfactory epithelium are significantly lower than the DNT flux as shown in Figures 4.5 and 4.6. However, amyl acetate and limonene are deposited more uniformly across the olfactory
epithelium where class II ORNs that are likely sensitive to insoluble odorants are predominantly expressed. In effect, the dog’s nose appears to utilize odorant absorption over a large surface area to compensate for the lower absorption rate of insoluble odorants. ORN density is approximately constant throughout the olfactory epithelium, so there are significantly more class II ORNs than class I ORNs in the nose (three times as many for the rat according to Schoenfeld and Cleland (2006)). Despite this, class I and class II ORNs converge to the same number of targets (glomeruli) in the olfactory bulb (Schoenfeld and Knott 2004; Schoenfeld and Cleland 2006). Thus, the high convergence ratio for class II ORNs and the absorption of insoluble odorants over the large olfactory surface area may act in concert to improve odorant “stimulus sensitivity” for insoluble odorants.

Most notably, epithelial flux patterns shown here correlate with ORN expression topography. ORNs that are sensitive to a particular class of odorants (soluble or insoluble) are located in regions where that class of odorants is deposited. This suggests that the epithelial flux patterns play an important role in odor recognition, especially for low-concentration odors where the efficient delivery of odorant molecules to ORNs is critical.

4.3.2 Relation to behavioral observations

Behavioral observations in rats and dogs suggest that sniffing is actively controlled during olfaction (Youngentob et al. 1987; Wesson et al. 2008a,b; Kepecs et al. 2007; Craven et al. 2009a; Settles 2005; Zuschneid 1973). Youngentob et al. (1987) found that rats sniffed more vigorously when presented with a weak (low-concentration) odor signal. Sniffing harder increases the airstream velocity in the nasal vestibule and dorsal meatus, thus
decreasing the fraction of the inspired odorant that is absorbed prior to the olfactory recess and increasing the total odorant flux to the olfactory recess (see Figure 4.7). Thus, it appears that macrosmatic mammals have evolved a sniffing strategy that provides a higher odorant flux to the ORNs in the presence of a weak odor signal.

4.4 Summary

Large-scale computational fluid dynamics simulations were performed to study the effect of odorant solubility, nasal airflow patterns, and nasal airflow rate on epithelial flux patterns in the canine olfactory recess. Our simulations show that odorant-laden air is transported directly to the olfactory recess via a high-velocity airstream, minimizing odorant loss through absorption on non-olfactory surfaces. The highly-soluble odorant DNT was observed to deposit only near the entrance to the olfactory region. Moderately-soluble amyl acetate and insoluble limonene were more evenly deposited across the olfactory epithelium and their flux patterns were influenced by both the olfactory airflow pattern and the nasal airflow rate.

Odorant flux patterns were found to correspond with ORN expression topography. Specifically, highly-soluble odorants are deposited in the olfactory region along the dorsal meatus where class I ORNs (sensitive to highly-soluble odorants) are expressed, whereas insoluble odorants are deposited across the entire olfactory recess where class II ORNs (sensitive to insoluble odorants) are predominately expressed. These results suggest that the nasal anatomy of the dog (and likely other macrosmatic animals) has evolved to
provide odorant flux patterns that complement the anatomical organization of ORNs in such a way as to enhance olfactory sensitivity and odor recognition abilities.
Chapter 5

CFD modeling of unsteady odorant transport

The time required for odorant molecules to diffuse across the mucus layer (≈ 0.1 s according to (Craven 2008)) is commensurate with the duration of a dog’s inspiratory sniff (≈ 0.1 s Craven et al. (2009a)). Therefore, temporal effects may significantly influence odorant transport patterns in the nasal cavity. To date, odorant transport during physiologically-realistic sniffing has not been studied in any animal, and it is therefore unknown if temporal effects on odorant transport patterns are significant.

When considering odorant transport during steady inspiration, it was possible to model mucus-phase transport using an air-phase boundary condition (see Chapter 4). Transient simulations are complicated by the fact that both air-phase and mucus-phase transport must be simulated simultaneously. This task requires a specialized mathematical treatment that is difficult to implement using commercial CFD codes, for which the source code is not typically available. Indeed, initial attempts to solve the unsteady transport problem with AcuSolve failed due to difficulty coupling the air-phase and mucus-phase simulations. Thus for the current purposes, recourse was taken in the open-source CFD code OpenFOAM (Open-Source Field Operation and Manipulation). Using OpenFOAM, a author-written CFD application (Conjugate Scalar Transport Foam - CSTFoam) capable of solving the unsteady odorant transport problem was developed. The remainder of this chapter describes the design of CSTFoam and reports the results of preliminary
simulations that were performed to verify it correctly solves the governing equations described in Chapter 3.

5.1 A brief overview of OpenFOAM

OpenFOAM is a C++ class library that was originally developed at the Imperial College of London in the 1990’s (see Jasak (1996) and Weller et al. (1998)) to solve CFD problems using the finite-volume method. OpenFOAM’s class library provides the functionality to perform mathematical operations that commonly occur in CFD algorithms (e.g. matrix algebra) using human-readable top-level code. Thereby, through manipulating relatively small amounts of code (generally less than 1000 lines), OpenFOAM’s class library can be used to discretize the governing equations of a problem over a computational domain, implement boundary conditions, and solve the resulting systems of algebraic equations. OpenFOAM is also distributed with several basic CFD applications (e.g. incompressible, compressible, multi-phase, and LES flow solvers), grid generation tools, and pre- and post-processing utilities.

5.2 Development of the OpenFOAM application

The author-written application CSTFoam considers all the physical phenomena of odorant transport during physiologically-realistic sniffing that were identified in Chapter 3. As illustrated in Figure 5.1, air-phase and mucus-phase odorant transport were simulated simultaneously in separate domains. Although CSTFoam is based on two standard
OpenFOAM CFD solvers (transientSimpleFoam and scalarTransportFoam), it contains 550 lines of author-written code. The author-written portions control the region-coupling algorithm (discussed in a later section) and implement the specialized air-mucus interfacial boundary condition required by Henry’s Law (Equation 3.4).

The flowchart presented in Figure 5.2 illustrates the algorithm used by CSTFoam to solve the unsteady odorant transport problem. A time-marching scheme is used to advance the solution from a set of initial conditions. At each timestep there are three main successive steps (emphasized in Figure 5.2) in the solution algorithm: Solve the nasal airflow field, solve the odorant concentration field in the nasal airways, and solve the odorant concentration field in the mucus layer.

Figure 5.1. A simplified schematic of the air-phase and mucus-phase computational domains used to simulate odorant transport in the canine nose. The physical phenomena considered in each domain and at the interfacial surface are listed. $C_{ai}$ and $C_{mi}$ are the air-phase and mucus-phase interfacial odorant concentrations, respectively.
Figure 5.2. Flowchart of CSTFoam illustrating the solution algorithm. Here, $n$ is an index that identifies the current sub-iteration loop, $\xi$ is a relaxation factor that is always less than 1, and $\varepsilon^n$ is the error in Henry's Law at the air-mucus interface.
5.2.1 Simulating airflow and odorant transport

As described in Chapter 3, the incompressible Navier-Stokes equations (Equations 3.1 and 3.2) govern airflow in the nasal cavity. These equations are discretized over the grid of the nasal airways and solved using a large-timestep ($Co > 1$) transient SIMPLE (Semi-Implicit Method for Pressure-Linked Equations) algorithm provided in OpenFOAM. The discretization methods are discussed in a later section.

The advection-diffusion equation (Equation 3.3) governs odorant transport in the nasal airways and the one-dimensional diffusion equation (Equation 3.6) describes odorant transport in the mucus layer. The linear nature of Equations 3.3 and 3.6 makes it possible to use a trivial solution algorithm. Both equations are discretized over their respective computational domains (using methods discussed in a later section), and the resulting systems of linear algebraic equations are solved using a preconditioned conjugate-gradient iterative solution method (Ferziger et al. 1999).

Given the linear differential equation that governs odorant transport in the mucus layer, it is possible to use an analytically solve for the mucus layer transport at each timestep. However, for the present problem implementing an analytical solution for mucus layer transport provided no advantage in terms of simulation speed. Further, it is not easy to utilize OpenFOAM's data organization structure to store the mucus phase odorant concentration field if an analytical solution is used. For these reasons, the use of an analytical solution was not practical. For completeness, the form of the analytical solution for the mucus layer is presented in Appendix B.
5.2.2 Region coupling algorithm

Given the airflow solution, a sub-iteration loop is used to implicitly couple the air-phase and mucus-phase simulations, as shown in Figure 5.2. The purpose of the sub-iteration loop is to ensure that Henry’s Law (Equation 3.4) and conservation of mass (Equation 3.5) are satisfied across the air-mucus interface. The first step in the sub-iteration loop is the simulation of air-phase odorant transport. The interfacial boundary condition for air-phase simulations within the sub-iteration loop is set using the mucus-phase interfacial concentration from the previous sub-iteration (or the previous timestep if it is the first pass through the sub-iteration loop) so that Henry’s Law is approximately satisfied,

\[ C_{ai}^n = C_{ai}^{n-1} + \xi (K_p C_{mi}^{n-1} - C_{ai}^{n-1}) \]  

(5.1)

Here, \( n \) and \( n - 1 \) are indices representing the current and previous sub-iteration loops, respectively. It is necessary to relax the boundary condition at the interfacial surface by a relaxation factor \( \xi < 1 \) to insure the stability of the region-coupling scheme. The value of the relaxation factor required is dependent on the partition coefficient of the odorant. For highly-soluble (DNT) and moderately-soluble (amyl acetate) odorants that have \( K_p \ll 1 \) it is possible to use a relaxation factor as high as \( \xi = 0.5 \). However, for insoluble odorants (limonene) that have \( K_p \approx 1 \) a relaxation factor \( \xi < 0.1 \) is required. Physically, this is because \( K_p \) values much smaller than 1 make the flux matching boundary condition for the mucus-phase simulations (Equation 3.5, see also Figure 5.2) more stable.
Next, using the resultant air-phase odorant concentration field, the odorant flux at the interfacial surface is calculated. This odorant flux is then applied as the interfacial boundary condition for mucus-phase odorant transport simulations, satisfying conservation of mass (Equation 3.5). After mucus-phase transport is simulated, the resultant mucus-phase interfacial surface concentration is used to provide the air-phase odorant concentration boundary condition (given by Equation 5.1) for the next sub-iteration, as shown in Figure 5.2. The sub-iteration loop is continued until Henry’s Law is satisfied to within a pre-defined tolerance.

\[ \varepsilon_{\text{tol}} \geq \left| C_{ai}^n - K_p C_{mi}^n \right| \]  

(5.2)

The \( \varepsilon_{\text{tol}} \) value used for the unsteady odorant transport simulations is discussed in Chapter 6.

### 5.2.3 The mucus-phase grid

The complex canine nasal anatomy precludes the generation of a mucus-phase grid that is body-fitted to the nasal airways. A schematic representation of a body-fitted grid is shown in Figure 5.3A. Specifically, the creation of a body-fitted mucus-phase grid requires that several thin prism layer are extruded from the surface of the air-phase grid. Three different meshing packages, Harpoon (Sharc Ltd.), ICEM (ANSYS Inc.),
and extrudeMesh (an OpenFOAM utility), were used in attempts to generate a body-fitted mucus-phase grid. These attempts were unsuccessful due to the thinness of the mucus layer and the sharp angles in the nasal airways (see Figure 1.1).

Fortunately, odorant transport in the mucus-phase is one-dimensional, and thus the only important mucus-phase grid dimension is the mucus layer thickness, $h_m$. It is therefore possible to use a two-dimensional mucus-phase grid that is not spatially coincident with the surface of the nasal airways to represent the highly three-dimensional mucus layer, as shown in Figure 5.3B. Note that odorant transport in the $y$-direction is not simulated because the transport phenomena in the mucus-phase are one-dimensional in the $x_n$-direction. To couple the air-phase and mucus-phase, the odorant surface concentration and flux are directly mapped between the two domains, and the number of air-phase and mucus-phase surface elements must therefore be the same.

![Figure 5.3](image.png)

Figure 5.3. Methods of coupling the air-phase and mucus-phase computational domains. (A) Coupled using a body-fitted mucus-phase grid. (B) Coupled using a mucus-phase grid that is not body-fitted.
5.2.4 Discretization schemes

Advection terms were discretized using a second-order-accurate total variation diminishing (TVD) scheme (see Roache (1998a)). In the present case, the use of a TVD scheme was required to ensure the solution remained stable. After testing three cell and face limiting TVD schemes, a face limited upwind discretization scheme was found to provide a stable solution. A second-order-accurate linear (central) discretization was used for all diffusion terms (Jasak 1996). Finally, a first-order-accurate Euler time discretization scheme was used (Jasak 1996). All of the second-order-accurate temporal discretization scheme that are implemented in OpenFOAM caused the solution to become unstable when used in conjunction with the face limited upwind TVD discretization scheme. As discussed in the next chapter, a timestep study was performed to insure the temporal accuracy of this first-order scheme was sufficient for the current purpose.

5.3 Verification of the OpenFOAM solver

A thorough verification of CSTFoam was performed to ensure that the governing equations of odorant transport were solved correctly. An analytical solution to the full set of governing equations is unavailable, thus CSTFoam was verified against a set of simplified airflow and odorant transport problems. Collectively, this set of problems verifies each term in the governing equations.
5.3.1 Verification of the airflow solution

The accuracy of the airflow solver was verified against the analytical solution to impulsively started flow in a circular pipe given in Equations 5.3-5.6 (White 1991).

\[ r_\ast = \frac{r}{r_o} \]  \hspace{1cm} (5.3)

\[ \lambda_n = \frac{(4n - 1) \pi}{4} \]  \hspace{1cm} (5.4)

\[ \tau = \frac{\nu t}{r_o^2} \]  \hspace{1cm} (5.5)

\[ \frac{u(r, t)}{u_{max}} = (1 - r_\ast^2) - \sum_{n=1}^{\infty} \frac{8J_0(\lambda_n r_\ast)}{\lambda_n^3 J_1(\lambda_n)} \exp \left(-\frac{\lambda_n^2 \tau}{4}\right) \]  \hspace{1cm} (5.6)

Here, \( u(r, t) \) is the axial velocity in the pipe, \( u_{max}(t) \) is the centerline velocity at any given time \( t \), \( \tau \) is the nondimensional time, \( r_o \) is the radius of the pipe, \( r \) is the radial coordinate measured from the center, \( r_\ast \) is the normalized radial coordinate, and \( J_0 \) and \( J_1 \) are Bessel functions of orders 0 and 1, respectively. Figure 5.4 compares the numerical results to the analytical solution. There is excellent agreement between the solutions, verifying that diffusive and temporal terms are correctly simulated by the airflow solver in an unsteady-flow situation.
Figure 5.4. Verification of the airflow solver.
5.3.2 Verification of air-phase odorant transport

5.3.2.1 Spatial accuracy

To verify the spatial accuracy of the transport terms in the advection-diffusion equation, the development of an odorant profile in a circular pipe was simulated. The boundary conditions for this simulation are specified in Figure 5.5. For these conditions, the analytical solution (see Shah and London (1978)) for the nondimensional odorant surface concentration, \( \theta \), is given by,

\[
Pe_{dh} = \frac{\bar{U}d_h}{D_{oa}}
\]

\[
\zeta = \frac{y}{2r_o} \frac{1}{Pe_{dh}}
\]

\[
\theta = \frac{C_a D_{oa}}{2q_s r_o} = \frac{11}{48} + 4\zeta + \frac{1}{2} \sum_{n=1}^{\infty} c_n \exp(-2b_n^2 \zeta)
\]

where \( q_s \) is the surface flux along the walls of the pipe, \( y \) is the axial coordinate, and \( b_n \) and \( c_n \) are eigenvalues given by Shah and London (1978). The nondimensional axial coordinate \( \zeta \) is defined here in terms of the Péclet number, \( Pe_{dh} \). Figure 5.6 presents a plot of \( \theta \) versus the \( \zeta \). The agreement between the analytical and computational solutions in the developing and fully-developed regions verifies the spatial accuracy of the air-phase odorant transport solution.
Figure 5.5. Boundary conditions for the steady advection-diffusion verification problem.

Figure 5.6. Verification of the spatial terms in the advection-diffusion equation.
5.3.2.2 Temporal accuracy

The temporal accuracy of air-phase odorant transport simulations was verified by simulating the advection of a step function odorant pulse through a circular pipe. For this simulation, the walls of the pipe were given a zero-odorant-flux boundary condition, the odorant diffusion coefficient was set to zero, and the velocity ($U$) in the pipe was uniform. The initial odorant concentration in the pipe was $C_a = 0$, and Equation 5.10 was specified as the inlet boundary condition.

$$C_a(t) = \begin{cases} 
0 & t < 0 \\
1 & t > 0
\end{cases} \quad (5.10)$$

The analytical solution to this problem is,

$$C_a(x, t) = \begin{cases} 
1 & x < Ut \\
0 & x > 0
\end{cases} \quad (5.11)$$

A comparison of the numerical and analytical solutions is presented in Figure 5.7. Numerical diffusion, that is inherent in the implicit temporal discretization and the TVD spatial discretization used here, caused the observed smoothing of the step function. In nature, this phenomenon also appears to a lesser extent, caused by physical diffusion. Given that sharp gradients of the type given by Equation 5.11 are not physical, the result shown in Figure 5.7 is deemed acceptable for present purposes.
Figure 5.7. Verification of transient advection in the air-phase.
5.3.3 Verification of mucus-phase odorant transport

The temporal and spatial accuracy of mucus-phase odorant transport simulations were verified using the analytical solution to one-dimensional transient diffusion (Truskey et al. 2008),

\[ \tau = \frac{t D_{om}}{h_m^2} \]  

(5.12)

\[ \eta = \frac{x_n}{h_m} \]  

(5.13)

\[ \theta = \frac{C_m(y) - C_o}{C_i - C_o} \]  

(5.14)

\[ \theta = 1 - 2 \sum_{n=0}^{\infty} \frac{(-1)^n}{(n + \frac{1}{2})\pi} \cos \left[ \left( n + \frac{1}{2} \right) \pi \eta \right] \exp \left[ - \left( n + \frac{1}{2} \right)^2 \pi^2 \tau \right] \]  

(5.15)

Here, \( \theta \) is the nondimensional odorant concentration, \( t \) is time, \( \tau \) is the nondimensional time, and \( \eta \) is the normalized mucus layer coordinate \( x_n \) (see Figure 5.1). This solution is for a mucus layer having an initial odorant concentration of \( C_o \), a zero-odorant-flux boundary condition at the epithelial surface, and an odorant concentration of \( C_i \) at the air-mucus interface. Figure 5.8 compares the computational and analytical solutions. The agreement between the solutions indicates that CSTFoam accurately simulates transient diffusion in the mucus layer.
Figure 5.8. Verification of transient diffusion in the mucus-phase.
5.3.4 Verification of the air-mucus interfacial boundary condition

A simple simulation was used to verify that CSTFoam satisfies Henry’s Law (Equation 3.4) and conservation of mass (Equation 3.5) at the air-mucus interface. Odorant transport was simulated in a two-dimensional channel with a mucus layer on the top and bottom surfaces. The odorant concentration at one end of the channel was specified as $C_a = 1$, and the concentration was specified to be $C_a = 0$ at the other. A sinusoidal pressure gradient was applied across the channel to create oscillating flow, representative of airflow in the canine nose during sniffing. Accordingly, the odorant concentration entering the channel was 1 or 0, depending on the flow direction. The boundary conditions at the air-mucus interfacial surfaces were specified to satisfy Henry’s Law and conservation of mass as described in Section 5.2.2, and the odorant concentration at the base of the mucus layers was set to $C_a = 0$.

Figures 5.9 and 5.10 compare computed odorant concentrations and fluxes integrated across the interfacial surfaces, respectively. The oscillations in the concentrations and fluxes correspond to the imposed sinusoidal changes in the flow direction as described above. The excellent agreement between the air-phase and mucus-phase odorant fluxes and concentrations proves that CSTFoam satisfies Henry’s Law and conservation of mass at the interfacial surface during unsteady odorant transport simulations.
Figure 5.9. Verification of Henry’s Law across the air-mucus interfacial surface.

Figure 5.10. Verification of conservation of mass across the air-mucus interfacial surface. Note that $J^*$ is the nondimensional odorant flux in units of $1/m^2\cdot s$ as defined in Chapter 3.
Chapter 6

Simulating odorant transport during physiologically-realistic sniffing

When a dog encounters an odor signal in nature, it ceases panting and begins sniffing at 5 Hz (Craven et al. 2009a). Thus far, odorant transport during steady inspiration has been considered in detail. However, a scaling argument in the previous chapter showed that the transient airflow caused by sniffing affects the odorant transport phenomena during olfaction. Thus, the CSTFoam CFD application is next used to study the unsteady odorant transport phenomena during physiologically-realistic sniffing.

6.1 Methods

6.1.1 Assumptions

Flow visualization experiments (Chapter 2) showed that turbulence in the nasal vestibule has little effect on the overall nasal airflow patterns. However, when the dog inspires an unmixed odor signal that might otherwise avoid entry into the olfactory region, turbulent mixing in the nasal vestibule ensures that a portion of the inspired odorant reaches the olfactory region. To simplify the odorant transport problem, the present simulations will consider the case of an odor signal that is well mixed prior to entering the nasal cavity. In this scenario, turbulence in the nasal vestibule has no effect on the odorant
transport phenomena, therefore all simulations will assume the nasal airflow is completely laminar. Other assumptions about the odorant transport phenomena during olfaction are thoroughly described in Chapter 3.

6.1.2 Boundary and initial conditions

6.1.2.1 Airflow

The air-phase computational domain consists of the canine nasal airway and two large plenums, as shown in Figure 6.1. The rostral plenum ensures that boundary effects do not influence the airflow entering the nasal cavity (Taylor et al. 2009). Initial simulations were performed without the caudal plenum by applying boundary conditions directly at the exit of the nasopharynx. This resulted in a “poorly-posed” set of airflow boundary conditions that did not satisfy the Navier-Stokes equations and caused the airflow solution algorithm to become unstable. To remedy this problem, the caudal plenum was added to the computational domain so that a “well-posed” set of far-field airflow boundary conditions could be specified.

When the dog sniffs, it expands and contracts its diaphragm at 5 Hz, creating an oscillating pressure gradient across the nose that induces nasal airflow. This was simulated by fixing the pressure across the front face of the rostral plenum, while sinusoidally oscillating the pressure across the back face of the caudal plenum (see Figure 6.1). The magnitude of the pressure oscillations ($p_{max}$) was specified such that the maximum inspiratory nasal airflow rate during the simulated sniff cycle was in agreement with the
physiologically-realistic value (Chapter 2). Air in the nose at the beginning of the simulations was specified to have an initial velocity of zero, although this initial condition is not particularly important because the nasal airflow is quasi-steady during sniffing (Craven et al. 2009a).

6.1.2.2 Odorant transport

To simulate the dog encountering an odor signal, the odorant concentration in the rostral plenum was given an initial value of $C_a = 1$ while all other regions of the computational domain were assigned an initial concentration of $C_a = 0$. During the sniff cycle, additional air that entered the rostral plenum was also specified to have a concentration of $C_a = 1$. Airflow entering the nasal cavity through the nasopharynx during expiration does not enter the olfactory region, and was observed to have little effect on odorant deposition patterns. Thus, for simplicity, a zero-gradient odorant boundary condition was applied across the back surface of the caudal plenum.

A two-dimensional grid was used to simulate odorant transport in the olfactory mucus layer as described in the previous chapter. Henry’s Law and conservation of mass were satisfied at the air-mucus interface in the olfactory region (defined in Figure 1.1) by the CSTFoam solver, thereby coupling air-phase and mucus-phase odorant transport. In accordance with the present assumptions, diffusion-limited odorant clearance at the epithelial surface was adopted, whereby the surface concentration across the bottom surface of the mucus-phase mesh was set to $C_a = 0$. Odorant deposition along the respiratory airways is not considered in the present odorant transport model, as discussed
Figure 6.1. Schematic illustration of the computational domain for unsteady odorant transport simulations, showing both the air-phase and mucus-phase boundary conditions.
in Chapter 3, and all the respiratory surfaces in the nose were given a zero-odorant flux boundary condition.

6.1.3 Grid generation

Harpoon (Sharc Ltd.) was used to generate hexahedral-dominant unstructured grids of the air-phase computational domain. Grids of 23 (coarse), 42 (medium), and 76 (fine) million elements were generated for use in a grid dependence study. The grid resolution was specified by assigning the size of surface elements on the nasal airways and an overall grid expansion ratio. A skewness-based smoothing algorithm (Sharc Ltd.) was used to optimize the grid quality. Due to the complex nasal geometry, several hundred elements along the walls of the nasal airways retained skewness ratios of over 0.95. Left alone, these elements caused airflow simulations to become unstable, therefore, these highly skewed elements were “blanked” using the CSTFoam solver, whereby the airflow velocity was forced to zero within the these elements. Element blanking effectively added a negligible amount of thickness ($\lesssim$ 50 µm) along some of the nasal airways and had no significant effect on the airflow solution.

Preliminary simulations were performed to determine the minimum number of mucus-phase elements required in the $x_\mu$-direction (see Figure 6.1). By way of the transient diffusion verification study presented in Section 5.3.3, it was found that 10 mucus elements sufficiently resolved the unsteady diffusion phenomena in the mucus layer.

The blockMesh OpenFOAM utility was used to generate the grids of the mucus-phase. The coarse, medium and fine air-phase grids contained 2.5, 4.8, and 8.2 million surface
elements in the olfactory region, respectively. Being 10 elements thick, the corresponding mucus layer meshes contained 25, 48, and 82 million elements.

### 6.1.4 Numerical solution

CSTFoam was used to numerically solve the governing equation of odorant transport during 5 successive sniff cycles (1 second of 5 Hz sniffing). For all simulations, the region-coupling convergence criterion was set to $\varepsilon_{\text{tolerance}} = 0.0001C^m_a$ (see Chapter 5). Typically, 10-20 region-coupling sub-iterations were required at each timestep to satisfy this condition. To keep the required computational time within reason, the maximum number of sub-iteration loops was specified to be 50. After 50 sub-iterations the region-coupling convergence criterion was satisfied during approximately 85% of the timesteps. A review of the computational results showed that during timesteps when the sub-iteration loop was stopped after 50 sub-iteration and the convergence criterion was not satisfied, the solution was always converged to within at least $\varepsilon \approx 0.01C^m_a$. Further converging the solution would not significantly change the results or conclusions of this study, thus the level of convergence achieved here is deemed acceptable for the current purpose.

All simulations were performed on 10 nodes of a parallel computer cluster, each node containing eight 2.8 GHz Intel Nehalem CPUs and 24 GB of RAM. Simulating odorant transport during 5 sniff cycles using the coarse grids required approximately 8000 CPU-hours (100 hours of real time) for DNT and amyl acetate. These simulations approached the limits of CPU-hours available for this project.
The transport of limonene took significantly longer to simulate because a low relaxation factor for the interfacial boundary condition (Equation 5.1) was required, as described in Chapter 5. Simulations of limonene transport were halted after 10000 CPU-hours (approximately three sniff cycles into the simulation) and the results were reviewed. It was determined that nothing further could be learned from simulating additional sniff cycles, thus it was not justified to use additional computational resources to complete the simulation of limonene transport.

6.2 Verification

6.2.1 Grid dependence study

Quantitative methods of calculating numerical error in CFD solutions, e.g. Richardson Extrapolation Analysis (REA) (Roache 1998b), provide accurate estimates of error if structured grids are used, where the grid resolution can be systematically increased. Error estimates are less reliable if unstructured grids are used, for which uniformly increasing the grid resolution is an ill-defined task. Thus, in the present case, simple qualitative and quantitative comparisons of the CFD airflow solution on different resolution grids are used to perform a grid resolution study.

The qualitative characteristics of the airflow patterns in the respiratory and olfactory regions were markedly similar for the coarse, medium, and fine grids, as shown in Figure 6.2. However, fine details of the airflow were better resolved as the grid resolution was increased, particularly in regions of high airflow velocity. The airflow solutions were
quantitatively compared by calculating the total nasal airflow rate for each grid. As Table 6.1 shows, increasing the grid resolution from 23 million cells to 76 million cells only slightly (<2%) changed the total nasal airflow rate.

<table>
<thead>
<tr>
<th>Grid</th>
<th>Number of grid elements (million) $N_i$</th>
<th>Peak inspiratory airflow rate (L/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coarse</td>
<td>23</td>
<td>0.437</td>
</tr>
<tr>
<td>Medium</td>
<td>42</td>
<td>0.442</td>
</tr>
<tr>
<td>Fine</td>
<td>76</td>
<td>0.445</td>
</tr>
</tbody>
</table>

Based on the results of this grid refinement study, it was determined that the additional computational resources required to use the medium and fine air-phase grids was not justified, hence the coarse 23-million-element grid was used for all simulations. Also note that the Schmidt number ($Sc_a = \nu/D_{oa}$) in the nasal airways is approximately 2.5 for all three odorants considered here, indicating that momentum is more diffusive than odorant mass in the air-phase. It follows that the air-phase grid resolution required to resolve nasal airflow is finer than the grid resolution required to resolve odorant transport. Thus, odorant transport in the air-phase was also sufficiently resolved by the coarse 23-million-element grid.
Figure 6.2. (A) Examples of grid resolution in the dorsal meatus. (B) Respiratory airflow patterns in the maxilloturbinate airways and the dorsal meatus for each grid. (C) Olfactory airflow patterns for each grid.
6.2.2 Timestep study

The airflow solution algorithm required a timestep of $dt \leq 0.0005$ seconds to achieve a stable airflow solution using the 23 million element grid. Any timestep larger than $dt = 0.0005$ seconds caused the solution to become unstable, even when relaxation factors for pressure and velocity were significantly reduced. For $dt = 0.0005$ seconds, the average Courant number across all grid elements at peak inspiration was $C_o = 0.28$, although several thousand elements in the nasal vestibule had Courant numbers on the order of 100.

Simulations were preformed at $dt = 0.0005$ and $dt = 0.0001$ seconds to determine if the transient characteristics of nasal airflow were sufficiently captured with the larger timestep. Figure 6.3 presents the time-histories of the total nasal airflow rate during the sniff cycle and Figure 6.4 compares the nasal airflow patterns in the respiratory and olfactory airways at peak inspiration for each timestep. Both comparisons show excellent agreement, demonstrating that a timestep of $dt = 0.0005$ seconds sufficiently resolves transient nasal airflow and odorant transport.

6.3 Results

6.3.1 Nasal airflow patterns during sniffing

The time-histories of the nasal airflow rate and pressure drop across the nasal cavity during the sniff cycle are shown in Figure 6.5. The airflow rate and pressure drop are
Figure 6.3. Time-history of the total nasal airflow rate during the sniff cycle for each timestep considered. Every $15^{th}$ timestep is plotted for $dt = 0.0001$ seconds.
Figure 6.4. Airflow patterns in the (A) respiratory airways and (B) olfactory airways at peak inspiration (0.05 seconds into the sniff cycle) for each timestep considered.
closely correlated (i.e. the airflow rate does not lag the pressure drop), indicating that the airflow is quasi-steady. In the present case, quasi-steady airflow was expected, because the Womersley number is approximately 1 in the vast majority of the nasal airways (Craven et al. 2007). Accordingly, the instantaneous airflow patterns during both inspiration and expiration are qualitatively indistinguishable from the steady airflow patterns described in Chapters 2 and 4. Beyond those discussions, the nasal airflow patterns are briefly described here.

Figure 6.5. Time-history of the nasal airflow rate and pressure drop during the sniff cycle.
Figure 6.6 illustrates the instantaneous airflow patterns at peak inspiration and expiration. Respiratory airflow, which comprises approximately 85% of the total airflow rate, travels ventrally through the maxilloturbinate airways and exits the nasal cavity at the nasopharynx, completely bypassing the olfactory region. The remaining 15% of the inspired airflow is advected quickly along the dorsal meatus to the rear of the olfactory region. From there, it turns 180 degrees and filters slowly forward through the large volume of the ethmoidal scroll-work towards the nasopharynx, where it exits the nasal cavity.

On expiration, all airflow enters the nasal cavity through the nasopharynx and flows directly through the maxilloturbinate airway, bypassing the olfactory region entirely. Thus, during expiration the olfactory airflow is quiescent, as shown in Figures 6.5 and 6.6.

These nasal airflow patterns cause unidirectional flow into the olfactory region that is pushed farther and farther through the ethmoidal scroll-work (see Figure 1.1) during the inspiratory portion of each sniff, until it is finally ejected to the nasopharynx. As described in Chapter 2, the time required for olfactory airflow to exit the nasal cavity varies between 1 and ~10 sniff cycles, depending on the specific olfactory flow path.
Figure 6.6. Contours and vectors of velocity in the z-direction in the dog’s nose during peak inspiration and peak expiration. The dashed lines indicate the general airflow path. Note that the velocity scales are different in the respiratory and olfactory regions.
6.3.2 Odorant transport during the sniff cycle

6.3.2.1 Total odorant flux to the olfactory epithelium

During the inspiratory portion of each sniff, odorant-laden airflow with a concentration $C_a = 1$ enters the olfactory region through the dorsal meatus, diffuses across the mucus layer, and is consumed at the epithelial surface by ORNs. During the expiratory portion of the sniff, no additional odorant enters the olfactory region, however, odorant continues to be absorbed and consumed, further depleting odorant molecules from the air “trapped” in the olfactory region.

The most basic measure of odorant transport during olfaction is the total amount of odorant consumed by ORNs. Here, this quantity is represented by the odorant flux integrated across the simulated epithelial surface at discrete times during the sniff cycle. Figure 6.7 presents the time-histories of the integrated odorant flux for DNT (highly-soluble), amyl acetate (moderately-soluble), and limonene (insoluble). The scale of the y-axis (total epithelium flux) in Figure 6.7A was specified to match Figure 4.7, which illustrates the integrated odorant flux during steady simulations. From Figure 6.7, four important characteristics of the unsteady odorant transport phenomena in the canine nose are immediately apparent:

1. The total epithelium fluxes are closely correlated with the nasal pressure drop and the nasal airflow rate, although the times at which the maximum odorant fluxes occur lag the maximum nasal pressure drop and airflow rate by approximately 0.075
seconds (note that one full sniff cycle lasts 0.2 seconds). This latency is associated with the time required for odorant to diffuse across the mucus layer.

2. The total epithelium flux increases with increasing odorant solubility (decreasing $K_p$).

3. During the expiratory portion of the sniff, while the olfactory airflow is quiescent, the epithelium flux decreases. Nevertheless, odorant is still absorbed by the epithelium, so olfaction is still occurring during the expiratory phase.

4. The epithelium flux patterns are temporally fully-developed (i.e. the patterns do not change with successive sniffs) for DNT and amyl acetate after a single sniff cycle, whereas the flux pattern for limonene continues to develop for at least three sniff cycles. Physically, this is because the rate of odorant absorption and consumption for DNT and amyl acetate is fast enough to balance the amount of odorant that enters the olfactory region during each inspiration. Conversely, the amount of limonene absorbed and consumed during the sniff cycle is quite small compared to the total amount of limonene that enters the olfactory region during each inspiration.

6.3.2.2 Detailed odorant transport patterns

The time-histories of the total odorant flux (Figure 6.7) provide valuable insight into the overall characteristics of odorant transport during olfaction, however, details of the spatial flux distribution patterns on the olfactory epithelium are not revealed by this
Figure 6.7. (A) Total odorant flux to the epithelium during the sniff cycle for all three odorants. (B) Total limonene flux to the epithelium on a rescaled y-axis.
global parameter. Thus, three different data visualization methods were used to further study the complex odorant transport phenomena in the canine nose:

1. Transverse cross-sections of odorant concentration in the olfactory airways were generated to visualize air-phase odorant transport. Figure 6.8 presents these cross-sections for each odorant at peak inspiration and peak expiration.

2. Contours of odorant flux across the olfactory epithelial surface were used to visualize the ORN odorant consumption patterns. For each odorant, four contours were generated at times during the simulations identified by the dashed lines labeled A-D in Figure 6.9. Figures 6.10, 6.11, and 6.12 present the epithelium flux contours for DNT, amyl acetate, and limonene, respectively. In these three figures, the olfactory region is viewed from the caudal end of the nose, looking towards the nasal septum (see Figures 1.1 and 1.2 for reference). The gray surfaces are non-absorbing respiratory airways and the external nose (seen from behind) is visible at the far left of each image. Also, it is important to note that the odorant flux scales in Figures 6.10-6.12 vary over three orders of magnitude. Specifically, the flux scales for amyl acetate and limonene are one and three orders of magnitude lower than the DNT scale, respectively.

3. Epithelium flux “probes” were used to study odorant flux throughout the sniff cycle at the specific locations annotated in Figure 6.13A. Figures 6.13B and 6.13C present the odorant flux time-histories for these probes on logarithmic y-axes.
During inspiration, the air-phase concentration and epithelial flux is highest along the dorsal meatus and nasal septum (see Figure 6.8, frames B and D in Figures 6.10-6.12). As airflow is advected farther into the olfactory region, both the air-phase concentration and the epithelial flux are observed to decrease. The degree to which this occurs is directly related to the solubility of the odorant in the mucus layer. Highly soluble odorants (exemplified by DNT) are rapidly depleted from the olfactory airflow by absorption and consumption along the dorsal meatus and the nasal septum (Figure 6.8). Insoluble odorants (exemplified by limonene) are less readily absorbed and consumed and are advected throughout the ethmoidal scroll-work at high concentrations (Figure 6.8). As a result, DNT exhibits a high epithelium flux in the vicinity of the dorsal meatus (i.e at the beginning of the olfactory region), but no flux to other olfactory surfaces (Figure 6.10). The epithelium flux of limonene is significantly lower, but is distributed across most of the epithelial surface (Figure 6.12). The inspiratory transport patterns for moderately-soluble odorants (exemplified by amyl acetate) fall between these two extremes.

During expiration, the olfactory airflow is quiescent and odorant already in the olfactory region is further absorbed into the mucus layer and consumed at the epithelial surface (Figure 6.8, frame C in Figures 6.10-6.12). The degree of odorant depletion is directly correlated with the solubility of the odorant. Nevertheless, as Figure 6.7 clearly illustrates, the amount of odorant flux to the epithelial surface never approaches zero during the sniff cycle, even for the most soluble odorants which are readily depleted from the olfactory airstream.
DNT and amyl acetate odorant transport patterns are effectively temporally fully-developed after a single sniff cycle. This is seen in Figures 6.10 and 6.11, where the differences between frames A and C and between frames B and D are insignificant. Conversely, limonene advects farther and farther into the olfactory region with each successive sniff, as Figure 6.12 shows. Based on the flow visualization experiments presented in Chapter 2, it takes more than 10 sniff cycles for limonene to fill the entire olfactory region. Once this happens, the limonene odorant transport patterns would be temporally fully-developed and would closely resemble the transport patterns predicted by the steady odorant transport simulations discussed earlier (Figures 4.5 and 4.4). Therefore, many sniffs may be required to detect low concentrations of insoluble odorants that require deposition over a large olfactory surface area to “amplify” the electrical signal sent to the brain (Schoenfeld and Cleland 2005).

**Epithelium flux probes** The six probe locations (Figure 6.13A) were chosen strategically at different points along the olfactory airflow path. Probes a, b, and c are along the dorsal meatus and the nasal septum near the entrance to the olfactory region, whereas probes 1, 2, and 3 are located in the ethmoidal scroll work, much farther into the olfactory airflow path (see Figure 4.3). In all cases, the epithelium flux oscillates at 5 Hz, while lagging the nasal airflow rate and pressure drop as described above. The epithelium flux time-histories at the probe locations are qualitatively similar to the total epithelium flux time-histories presented in Figure 6.7.

Figure 6.13B presents the epithelium flux time-histories for probes a, b, and c. The flux at probe a is always higher than the fluxes at probes b and c, principally because probe
a is located at the beginning of the olfactory airflow path where the air-phase odorant concentration is highest. DNT is readily absorbed and its epithelium flux is seen to decrease quickly along the airflow path between probes a and c. Amyl acetate is less soluble in the olfactory mucus, thus the amyl acetate flux is lower, but more uniform along the olfactory airflow path. It is interesting to note that the flux at probe location c peaks slightly earlier (by $\sim 0.0125 \text{ s}$) than at probe locations a and b. This somewhat confusing behavior is the result of an early peak in odorant availability at probe c due to small changes in the olfactory airflow path during the course of a sniff.

Probes 1, 2, and 3 (Figure 6.13B) are located in a region of low airflow velocity in the ethmoidal scroll-work. Probe 1 is near the entrance to the scroll-work, whereas probes 2 and 3 are located in the scrolls. A small amount of DNT flux is recorded at probe 1, but almost no DNT reaches the ethmoidal scroll-work, thus probes 2 and 3 record a negligible DNT flux. The amyl acetate odorant concentration in the ethmoidal scroll work is significantly higher than the DNT concentration (Figure 6.8). As a result, the amyl acetate flux at probes 1, 2, and 3 is always higher than the DNT flux at the corresponding location.

6.4 Discussion

The results from the steady odorant transport simulations presented earlier in Chapter 4 show that the odorant flux patterns across the olfactory epithelium are closely correlated with the anatomical organization of ORNs in the olfactory region. The present results
Figure 6.8. Transverse cross-sectional contours of odorant concentration in the olfactory region at peak inspiration (0.05 seconds into the sniff cycle) and peak expiration (0.15 seconds into the sniff cycle).
Figure 6.9. The temporal location of the epithelium flux contours presented in Figures 6.10-6.12. The dashed lines A-D correspond to the labels in each figure.
Figure 6.10. Contours of DNT flux across the olfactory epithelial surface. Frames A-D were extracted at times during the sniff cycle identified by the dashed lines in Figure 6.9.
Figure 6.11. Contours of amyl acetate flux across the olfactory epithelial surface. Frames A-D were extracted at times during the sniff cycle identified by the dashed lines in Figure 6.9.
Figure 6.12. Contours of limonene flux across the olfactory epithelial surface. Frames A-D were extracted at times during the sniff cycle identified by the dashed lines in Figure 6.9.
Figure 6.13. Epithelium flux at six different probe locations during the sniff cycle. (A) The probe locations. (B) Epithelium flux for probe locations a, b, and c. (C) Epithelium flux for probe locations 1, 2, and 3.
show that the odorant transport patterns during physiologically-realistic sniffing (Figures 6.8 and 6.10-6.12) are remarkably similar to those during steady inspiration (Figures 4.4 and 4.5). This is especially true for DNT and amyl acetate, which both have odorant transport patterns that are fully developed after a single sniff cycle.

Thus, regarding the spatial encoding of different odorants by the olfactory system, sniffing provides no apparent advantage. In fact, when compared with steady inspiration, sniffing actually reduces the amount of odorant delivered to ORNs under the present set of assumptions. This is because no odorant-laden airflow enters the olfactory region during the expiratory portion of a sniff. It therefore seems likely that sniffing has evolved more for the advantages it provides in terms of external trace sampling, as discussed further in Chapter 7.

Nevertheless, in the case of a strong odor signal, the act of sniffing may provide an olfactory advantage. Here, it is observed that one notable characteristic of canine sniffing is the quiescent airflow in the olfactory region during expiration (see also Craven et al. 2009a). During the quiescent period the odorant flux to the epithelium decreases, thus, the amount of odorant delivered to ORNs oscillates during the sniff cycle (Figures 6.7 and 6.13). This oscillation may prevent the “fast adaptation” (or desensitization) of ORNs to an odor signal (Lancet 1986; Ache 1991).
Chapter 7

Summary, conclusions, and future research

7.1 Summary

This dissertation studied the airflow and odorant transport phenomena during canine olfaction, with the goal of contributing to the fundamental understanding of the natural olfactory system while simultaneously learning biomimetic design principles to improve artificial olfaction devices. In this endeavor, a set of flow visualization experiments and computational simulations were performed.

An anatomically-correct experimental model of the canine nose was designed and fabricated using a rapid prototyping technique. This model was used in a set of novel flow visualization experiments to characterize canine nasal airflow. The results of these experiments were used to study flow phenomena that are difficult to investigate with CFD techniques, and also to provide validation for CFD simulations of nasal airflow.

Next, a mathematical model of odorant transport during olfaction was developed. This model was solved computationally under two different sets of assumptions. Odorant transport was first simulated under the simplifying assumption that the airflow in the dog’s nose is steady. Finally, a custom-written CFD application was used to simulate
unsteady odorant transport for the physiologically-realistic case of unsteady (sinusoidal) canine sniffing.

7.2 Conclusions

7.2.1 Contributions to the basic science of olfaction

When performing olfactory tasks, the dog actively sniffs, whereby odorant molecules are transported from the external environment to ORNs in the olfactory region of the nose. Previous research suggests that the nasal anatomy of macrosmatic mammals and the act of sniffing are optimized by evolution for the efficient trace sampling of the external environment (Settles et al. 2003; Settles 2005). The results presented in this dissertation support the hypothesis (Craven et al. 2009a) that these factors also result in internal nasal airflow and odorant transport patterns that efficiently deliver odorant molecules to ORNs in the canine olfactory region. In the remainder of this section, the implications of the present results are discussed in respect to the basic science of the function of the dog’s olfactory system.

The flow visualization experiments show that inspired odor signals are well-mixed by vortex shedding and turbulence in the nasal vestibule before the nasal airflow splits into separate respiratory and olfactory airflow paths. In a natural environment, this mixing ensures that a portion of any inspired odor signal enters the olfactory flow path and thence reaches the olfactory region.
During the inspiratory portion of a sniff, olfactory airflow is delivered to the rear of the olfactory region via a high-velocity air stream flowing through the dorsal meatus, thus minimizing odorant absorption on other non-olfactory surfaces prior to the olfactory region. The present CFD simulations of odorant transport show that this odorant delivery mechanism is of particular importance for the detection of highly-soluble odorants (exemplified by DNT) that are readily absorbed upon inspiration.

In the olfactory region, airflow becomes completely laminar and is exposed to the large surface area of the scroll-like ethmoturbinates, in which ORNs are located. Because olfactory airflow is stagnant on expiration, airflow that enters the olfactory region must traverse a tortuous path through the ethmoturbinates over several sniff cycles before eventually exiting at the nasopharynx. This olfactory airflow pattern enables the “chromatograph-like” separation of odorants, whereby odorant molecules are deposited non-uniformly along the mucus-lined nasal airways. The present CFD simulations show that deposition patterns are odorant-specific and are determined by the olfactory airflow pattern and the odorant solubility in the mucus layer. These deposition patterns are correlated with the expression topography of ORNs in the rat (Schoenfeld and Cleland 2005), which is presumably similar to that of the dog. Thus, odorant deposition patterns likely play a critical role in odor discrimination.

The rapid sniffing (at approximately 5 Hz) exhibited by dogs during olfaction is not found to be advantageous regarding the spatial encoding of odorants. Specifically, sniffing does not change the odorant deposition patterns compared to steady inspiration (except possibly for insoluble odorants), and in fact it decreased the amount of odorant delivered
to the olfactory region. However, in the case of strong odor signals, sniffing may decrease the probability that ORNs are desensitized (Lancet 1986; Ache 1991) by a constant odor stimulus. In the case of a weak odor signal, sniffing may be most advantageous in regards to external aerodynamic sampling. Specifically, when a dog sniffs a surface, the expired air-jets from its nostrils disturb fine particulates in the vicinity of an odorant sources (Settles et al. 2003). In situations where inaccessible or weak odor signals are encountered, dog’s have been observed to use a “long sniff” of approximately 1/3-1/2 Hz (Settles et al. 2003; Zuschneid 1973; Morrison 2000; Settles 2005). Both the “long sniff” and the normal 5Hz sniff appear to maximize the amount of odorant delivered to the olfactory region in the case of a weak odor signal.

Dogs rely on their sense of smell for survival, therefore their ability to effectively detect trace odor signals is critical. It appears that the nasal anatomy and behavioral traits of the dog (and likely other macrosmatic animals) have evolved to maximize olfactory sensitivity, at least from a fluid dynamics and odorant mass transport perspective. Conversely, microsmatic species (e.g. humans) rely less on their sense of smell for survival and have evolved a markedly less-sophisticated nasal cavity that is not optimized for olfaction (Craven et al. 2009a).

7.2.2 Significance to the design of bio-inspired artificial olfaction devices

While significant effort has been invested in the development of highly-sensitive chemical sensors (Steinfeld and Wormhoudt 1998; Pinnaduwage et al. 2003; Moore 2004; White
et al. 1998, 2008), the aerodynamic sampling devices that are required to deliver odor signals to sensor surfaces are typically given secondary importance. Lessons learned from nature on the aerodynamic design of an artificial olfaction device were earlier summarized by Settles (2005), especially the need for a large sensory surface area and frictional pressure loss to maximize the chance of odorant molecules contacting the sensors. Here we see three additional functional advantages provided by the behavior and nasal anatomical structure of the canine that should be considered in the design of future artificial olfaction devices:

1. The laminar olfactory airflow causes odorant-specific deposition patterns over the large olfactory surface area, with specialized ORNs presumably distributed across it selectively (as in the rat) for maximum advantage. This provides the dog an opportunity to separate the components of a complex scent, as in chromatography, in order to improve neurological olfactory pattern recognition. To date, apparently no electronic nose designs have taken advantage of this “chromatographic” effect.

2. Turbulent mixing in the nasal vestibule ensures that odor signals are well-mixed before they reach the olfactory region, increasing the chance that all inspired odor signals are interrogated.

3. In the case of a strong odor signal, sniffing delivers a temporally-varying odor signal to the olfactory region, likely preventing the desensitization of the dog’s ORNs.

The compromise of olfaction and respiration in the limited volume of the dog’s nose requires airborne conveyance of odorants to the olfactory recess at the rear of the nasal
cavity before olfaction can occur. The potential loss of trace chemicals to the walls of conveyance tubes is well known. Highly-soluble odorants with small partition coefficients are the first to be absorbed into the mucus layer, and some may not even reach the dog’s olfactory epithelium. Thus, it appears the dog’s nose is not optimized to detect highly-soluble odorants (including some explosives) which are quickly absorbed upon entering the nasal cavity. Nonetheless, the lessons learned here can be applied to bio-inspired artificial olfaction devices, where a compromise with respiration is no longer required, and where the nose design can target the chemical properties (e.g. solubility) of specific odorants of interest.

7.3 Future research

Recommendations for the direction of additional future research related to canine olfaction are given below in terms of experimental and computational efforts.

7.3.1 Experimental measurements

1. In this research, the air-mucus equilibrium partition coefficients \(K_p\) and mucus diffusivities \(D_{om}\) of the three odorants considered were estimated using the equivalent air-water values. However, recent research (Kurtz et al. 2004) suggests that these properties, especially the \(K_p\) value, are significantly influenced by the heterogeneous nature of the olfactory mucus layer. The present results show that \(K_p\) values strongly influence odorant transport patterns in the canine nasal airways.
(see Chapters 4 and 6). Therefore, accurate $K_p$ and $D_{om}$ values for actual canine mucus should be determined experimentally and used in future studies of odorant transport during olfaction.

2. Settles et al. (2003) showed that the external naris expands and contracts during the sniff cycle. Specifically, video recordings show that a pathway that leads to the dorsal meatus dilates during inspiration, possibly influencing the distribution of airflow to the olfactory region. The motion of the external naris during the sniff cycle should be fully characterized using stereoscopic video recordings and the effect of the motion on nasal airflow should be studied. Naris motion could potentially increase the percentage of inspired airflow that reaches the olfactory region.

3. The feasibility of fabricating an optically-transparent experimental model of the canine nasal airway that allows PIV measurements should be investigated.

4. The possibility of making in-vivo measurements of canine nasal airflow using MRI velocimetry (Bonn 2009) should also be considered.

### 7.3.2 Computational simulations

1. It is possible that inspired particles play an important role in odor detection, especially for non-volatile materials. Lagrangian particle tracking CFD simulations should be performed to determine the role (if any) of particles and aerosols in olfaction. A CFD study is appropriate here, since this topic is difficult to study using live animals and experimental models.
2. Extend the computational model to include scalar odorant deposition in the respiratory region of the nose. Although not applicable to the study of olfaction, deposition in the respiratory region is certainly relevant in other fields of study (e.g. inhalation toxicology).

3. Incorporate the motion of the external naris described above into the computational model, in order to better simulate the actual portion of inspired airflow that reaches the olfactory region.
Appendix A - Refractive index matching experiments

Quantitative optical flow diagnostic techniques that are commonly used in fluid dynamics experiments (e.g. particle image velocimetry (PIV), laser Doppler velocimetry (LDV), and planar laser induced florescence (PLIF)) require experimental models that are transparent and free of optical distortions. Optical distortions are caused by the refraction of light as it passes across the interfacial surfaces between an experimental model and a working fluid that are not perpendicular to the direction of the light. In such cases, a common method of eliminating distortion due to refraction is to use a working fluid that has the same refractive index as the experimental model (e.g. Hendriks and Aviram 1982; Budwig 1994; Cui 1995; Cui and Adrian 1997; Hopkins et al. 2000; Narrow et al. 2000; de Zélicourt et al. 2005; Miller et al. 2006; Hassan and Dominguez-Ontiveros 2008).

In the current research, three steps were taken to determine the feasibility of using an index-matching fluid with the experimental model of the dog’s nose: (1) candidate fluids were identified, (2) experiments were performed to determine how well the refractive index of the candidate fluids could be matched to that of the model, and (3) the required flowrates for the candidate fluids were calculated to determine the cost and practicality of using an index-matched fluid in laboratory scale experiments. This appendix describes each of these steps.
Identification of candidate fluids

The refractive index of the PolyJet FullCure 720 material from which the experimental model of the dog’s nose was fabricated is \( n = 1.53 \), according to the manufacturer (Objet Geometries Ltd.). When the model is filled with air \( (n = 1.00) \) it is completely opaque due to refraction at the air-model interfacial surfaces, as Figure 7.1A shows. To reduce refraction, thus rendering the model more transparent, a fluid with an refractive index that is closer to the refractive index of the PolyJet material is required. It was also determined that an acceptable index-matching fluid must meet the following criteria:

1. Toxicity: Handling the fluid must not be hazardous to one’s health according to the materials safety data sheet.

2. Flammability: The fluid cannot be highly flammable according to the materials safety data sheet.

3. Reactivity: The fluid must not react with the PolyJet material or damage the experimental model. Specifically, it must not dissolve the PolyJet material.

4. Clarity: The fluid must be transparent.

5. Cost: The cost of the fluid cannot be excessive (i.e. the fluid cannot cost thousands of dollars).

Several candidate fluids were identified through a review of the literature. These fluids are presented in Table 7.1. To determine if the candidate fluids damage the PolyJet material,
small PolyJet test pieces were soaked in each fluid for 12 hours. Benzyl alcohol, methyl salicylate, and chlorobenzene dissolved the test pieces, whereas ammonium thiocyanate and potassium thiocyanate solutions turned the surfaces of the test pieces a pink color. The zinc iodide solution became yellow when exposed to air for an extended period (>1 hour). These chemicals were therefore rejected from the list of candidate fluids.

Water and Cargille OHZB fluid were the only fluids that were found to satisfy the established criteria. The refractive index of water \((n = 1.33)\) is approximately 13\% lower than the reported refractive index of the PolyJet material. Although the refractive index of water cannot be adjusted, the OHZB fluid can be ordered from Cargille-Sacher Laboratories (www.cargille.com) with refractive indices ranging between \(n = 1.465\) and \(n = 1.555\) in intervals of 0.005.

**Refractive index matching experiments**

A simple experiment was performed to match the refractive index of the OHZB fluid with the refractive index of the experimental model as precisely as possible. Identical test pieces of PolyJet material were submerged in OHZB fluids having \(n = 1.525, 1.530,\) and 1.535 in clear beakers with flat bottoms. The beakers were placed in a ring stand 15 cm above a grid consisting of alternating white and black lines with a line width of \(\sim 2\) mm. Each test piece was then photographed from above at a camera angle perpendicular to the grid (this constitutes a rudimentary background-distortion schlieren technique. If a perfect refractive index match between the PolyJet material and the OHZB fluid was
achieved, the grid should appear undistorted. Conversely, if the refractive index match is imperfect, refraction at the interface between the test part and the OHZB fluid will distort the lines of the grid. For comparison, the same experiment was also performed using water, which has an refractive index that is not a close match with the PolyJet material, as described above. The results from these experiments are presented in Figure 7.2.

From a careful inspection of Figure 7.2, it is seen that the least distortion occurred when the test piece was submerged in the OHZB fluid with \( n = 1.530 \). This indicates that the actual refractive index of the PolyJet material is \( n = 1.530 \pm 0.0025 \), a value that is in agreement with the refractive index reported by the manufacturer (Objet Geometries Ltd.).

However, even with the close refractive index match between the \( n = 1.530 \) OHZB fluid and the test piece, significant distortion of the grid lines is apparent in Figure 7.2. This distortion is apparently due to inhomogeneous optical properties between the thin layers that comprise PolyJet models. It is unknown if the inhomogeneities are due to small air bubbles, non-uniform stress concentrations between the PolyJet layers, or other properties of PolyJet models. Unfortunately, such inhomogeneities make achieving a perfect refractive index match between a fluid and a PolyJet part made of FullCure 720 resin impossible. Improving the uniformity of the optical properties of PolyJet parts by modifying the manufacturing process is likewise far beyond the scope of the present study and was therefore not considered.
Next, the transparency of the experimental model when filled with water and \( n = 1.530 \) OHZB fluid was considered (Figure 7.1). As expected, the model was most transparent when filled with the OHZB fluid, however, the majority of the internal airways were still visible when the model was filled with water. In both cases, it was not possible to pass a laser-beam through the model without significant distortion because of refraction and diffraction due to the imperfect refractive index match between the fluid (OHZB or water) and the PolyJet model. Based on this result, it was determined that traditional PIV or LDV measurements that require a distortion-free experimental model were not feasible. The optical quality of the PolyJet model is only acceptable for dye-flow visualization experiments and other flow measurements that do not require a model that is free of optical distortion.

Note that the maxilloturbinte region is not transparent even in OHZB, but fortunately the dorsal meatus and ethmoturbinate region are clear enough for good flow visualization even using water.

**Dynamic scaling**

Dynamic scaling calculations were performed (as described in Chapter 2) to determine the required flow rate for water and the OHZB fluid to simulate airflow through a live dog’s nose. Using Equation 2.2 it was found that the required water and OHZB flow rates are 0.14 L/s and 0.97 L/s at peak inspiration, respectively.
The type of flow visualization experiments that were used to study the nasal flow patterns require that a dye-streak is injected into the flow. Once the dye is injected, there is no way of separating it from the working fluid, thus a new batch of fluid is required for each experiment. Given that an OHZB flowrate of 0.97 L/s is required and OHZB fluid costs $140 per liter, flow visualization experiments using OHZB fluid were determined to be prohibitively expensive and were thus not performed. Fortunately, as Chapter 2 demonstrated, water-dye flow visualization experiments were sufficient for the purpose of studying flow patterns in the dog’s nose.
Figure 7.1. The experimental model of the dog’s nose filled with air, water, and Cargille OHZB fluid. Note that the nose model is made of PolyJet FullCure 720 resin with an experimentally-determined refractive index of $n = 1.530 \pm 0.0025$. 

Air, $n = 1.00$

Water, $n = 1.33$

OHZB, $n = 1.530$
Table 7.1. Candidate refractive index matching fluids and their properties. Levels of toxicity and flammability are ranked on a scale from 0–5 according to the material safety data sheet (MSDS) for each chemical. 0 is the lowest level.

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Index of refraction (IOR)</th>
<th>CAS #</th>
<th>Toxicity</th>
<th>Flammability</th>
<th>Reactivity</th>
<th>Density (kg/m³)</th>
<th>Kinematic viscosity x 10⁶ (m²/s)</th>
<th>Clarity</th>
<th>Approximate cost per liter ($)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>1.33</td>
<td>7732-18-5</td>
<td>0</td>
<td>0</td>
<td>No reaction</td>
<td>1000</td>
<td>1.12</td>
<td>Clear</td>
<td>0</td>
<td>Hendriks and Aviram (1982)</td>
</tr>
<tr>
<td>Zinc iodide aqueous solution</td>
<td>1.33-1.62 (at saturation, ~82% by mass)</td>
<td>10139-47-6</td>
<td>2</td>
<td>0</td>
<td>No reaction</td>
<td>1889-4031</td>
<td>1.12 - 9.61</td>
<td>Yellow tint</td>
<td>0-800</td>
<td>Budwig (1994)</td>
</tr>
<tr>
<td>Ammonium thiocyanate aqueous solution</td>
<td>1.33-1.5 (at saturation, ~56% by mass)</td>
<td>1762-95-4</td>
<td>2</td>
<td>0</td>
<td>Turned the PolyJet material a pink color</td>
<td>1000-1300</td>
<td>1.12 - 1.56</td>
<td>Clear</td>
<td>0-140</td>
<td>Budwig (1994)</td>
</tr>
<tr>
<td>Potassium thiocyanate aqueous solution</td>
<td>1.33-1.49 (at saturation, ~60% by mass)</td>
<td>333-20-0</td>
<td>2</td>
<td>0</td>
<td>Turned the PolyJet material a pink color</td>
<td>1000-1740</td>
<td>1.12 - 1.70</td>
<td>Clear</td>
<td>130</td>
<td>Budwig (1994)</td>
</tr>
<tr>
<td>Benzyl alcohol</td>
<td>1.54</td>
<td>100-51-6</td>
<td>2</td>
<td>1</td>
<td>Dissolved the PolyJet material</td>
<td>1044</td>
<td>1.89</td>
<td>Clear</td>
<td>150</td>
<td>Cui and Adrian (1997)</td>
</tr>
<tr>
<td>Cargille OHZB fluid</td>
<td>1.465 - 1.555</td>
<td>N.A.</td>
<td>1</td>
<td>0</td>
<td>No reaction</td>
<td>2324</td>
<td>7.85</td>
<td>Clear</td>
<td>140</td>
<td><a href="http://www.cargille.com">www.cargille.com</a></td>
</tr>
<tr>
<td>Methyl salicylate</td>
<td>1.53</td>
<td>119-36-8</td>
<td>2</td>
<td>0</td>
<td>Dissolved the PolyJet material</td>
<td>1184</td>
<td>2.99</td>
<td>Clear</td>
<td>140</td>
<td>Nguyen et al. (2004)</td>
</tr>
<tr>
<td>Chlorobenzene</td>
<td>1.53</td>
<td>108-90-7</td>
<td>3</td>
<td>3</td>
<td>Dissolved the PolyJet material</td>
<td>1110</td>
<td>0.81</td>
<td>Clear</td>
<td>70</td>
<td>Author-identified</td>
</tr>
</tbody>
</table>
Figure 7.2. Results from refractive index matching experiments.
Appendix B - Analytical solution for mucus layer transport

This Appendix presents an alternate solution method for determining the odorant concentration profile in the mucus layer during unsteady sniffing. This solution method could have been combined with the OpenFOAM solution for air-phase odorant transport. However, the semi-analytical solution presented in this Appendix does not allow for the OpenFOAM data structure to be used to store the odorant concentration field. Also, the time required to solve for odorant transport in the mucus layer using OpenFOAM was only approximately 2% of the total simulation time. Therefore, the solution method presented below was not implemented.

Semi-analytical solution for mucus-phase odorant transport

Given the differential equation that governs odorant transport in the mucus layer (Equation 7.1) an analytical solution is possible at each timestep.

\[
\frac{\partial C_m}{\partial t} = \frac{\partial C_m}{\partial x^2} \tag{7.1}
\]

If we choose an Euler implicit time discretization scheme that is consistent with the CFD simulations, the following linear differential equation results,

\[
\theta''_{n+1} - k\theta^{n+1} = \theta^n \tag{7.2}
\]
where, \( n \) and \( n + 1 \) represent the previous and current timesteps, respectively. In this case, the solution from the previous timestep (\( \theta^n \)) is a function of \( x \) and is known from previous calculations.

The solution to Equation 7.2 is formed from the summation of the homogeneous solution and a particular solution.

\[
\theta^{n+1} = \theta^{n+1}_h + \theta^{n+1}_p
\]  
(7.4)

The homogeneous solution takes the form,

\[
\theta^{n+1}_h = C_1 e^{\sqrt{kx}} + C_2 e^{-\sqrt{kx}}
\]  
(7.5)

where \( C_1 \) and \( C_2 \) are determined from boundary and initial conditions. To determine a particular solution for an arbitrary odorant concentration profile at the previous timestep, the domain can be discretized in the \( x \)-direction and \( \theta^n \) can be described in terms of a Fourier series determined via a Discrete Fourier Transform.

\[
\theta^n = a_0 + \sum_{m=1}^{NJ} a_m \cos(k_m j \Delta y) + \sum_{m=1}^{NJ} b_m \sin(k_m j \Delta y)
\]  
(7.6)

If \( \theta^n \) is an odd function with a period of twice the domain height,

\[
\theta^n = \sum_{m=1}^{NJ} b_m \sin(k_m j \Delta y)
\]  
(7.7)
\[ c_m y = k_m j \Delta y \] (7.8)

Thus, each mode of \( \theta^n \) can be written as,

\[ \theta^n_m = b_m \sin(c_m y) \] (7.9)

and each mode has a particular solution,

\[ \theta^{n+1}_{p,m} = -\frac{b_m}{c_m^2 + 1} \sin(c_m y) \] (7.10)

Therefore, the entire particular solution can be written as,

\[ \theta^{n+1}_p = \sum_{m=1}^{NJ} -\frac{b_m}{c_m^2 + 1} \sin(c_m y) \] (7.11)

Combining Equations 7.5 and 7.11 the complete solution is formed at each timestep,

\[ \theta^{n+1} = \sum_{m=1}^{NJ} -\frac{b_m}{c_m^2 + 1} \sin(c_m y) + C_1 e^{\sqrt{kx}} + C_2 e^{-\sqrt{kx}} \] (7.12)
Bibliography


Vita - Michael Lawson

Michael Lawson was born on May 24th, 1983, in Providence, Rhode Island, to James and Gail Lawson. Michael attended Ponaganset High School where he competed in Track and Field and Cross Country.

Following his High School graduation in 2001, Michael attended Virginia Tech, from where he graduated in 2005 with a B.S. in Mechanical Engineering. Michael continued his studies at Virginia Tech and received a M.S. in Mechanical Engineering in 2005 while studying under Dr. Karen Thole. The title of his M.S. thesis was “Practical Applications of Delta Winglets in Compact Heat Exchangers with Louvered Fins”.

After completing his M.S., Michael was a graduate intern at BMW in Munich, Germany, where he performed research related to improving vehicle aerodynamic performance.

Michael began his Ph.D. research under Dr. Gary Settles and Dr. Eric Paterson at The Pennsylvania State University in 2007. At Penn State, Michael worked in the Gas Dynamics Lab and at the Applied Research Lab, where he studied canine olfaction in an attempt to reverse engineer the dog’s nose.

Currently, Michael is a Post-Doctoral Researcher at the National Renewable Energy Lab where he studies efficient ways to extract energy from winds and ocean currents.