CURRICULUM VITAE
Mette Sofie Olufsen, PhD

PART I: General Information

Date: January 31st, 2007

Work Address: Department of Mathematics
Campus Box 8205
North Carolina State University
Raleigh, NC 27695

Telephone: 919 515 2678
Fax: 919 515 3798

Home Address: 1314 Pendula Path, Apex, NC 27502
Telephone: 919 362 5287

E-mail: msolufse@math.ncsu.edu
Website: http://www4.ncsu.edu:8030/~msolufse

Education:

1993 MSc Mathematics and Computer Science, Roskilde University, Denmark.
Thesis: *DISCO - DIScrete and COntinuous Simulation in Turbo Pascal*.

1998 PhD Applied Mathematics, Roskilde University, Denmark.
Thesis: *Modeling the Arterial System with Reference to an Anesthesia Simulator*.

Professional Appointments:

1994-1998 Industrial Researcher, Math-Tech, Copenhagen, Denmark.
1994-1998 Research Assistant, Department of Mathematics, Roskilde University.
1998-2001 Research Associate, Center for BioDynamics and Department of Mathematics, Boston University, Boston, MA.
2001-2006 Assistant Professor, Department of Mathematics, North Carolina State University, Raleigh, NC.

Other Professional Affiliations and Visiting Appointments:

1994 (fall) Visiting Research Assistant, Courant Institute of Mathematical Sciences, New York University, New York, NY.
1996 (spring) Visiting Researcher, School of Mathematics, Australian Defense Force Academy, University of New South Wales, Canberra, ACT, Australia.
1996 (fall) Visiting Research Assistant, Courant Institute of Mathematical Sciences, New York University, New York, NY.
2001-2006 Associate Faculty, Biomath Program, North Carolina State University, Raleigh, NC.
2002-2006 Associate Faculty, Department of Biomedical Engineering, North Carolina State University, Raleigh, NC.

Professional Societies:

1. Society of Industrial and Applied Mathematics (SIAM).

Peer Reviewed Journal Articles:

1. D. Valdez-Jasso, M.A. Haider, H.T. Banks, D. Bia, Y. Zocalo, R. Armentano, M.S. Olufsen. *Viscoelstic mapping of the arterial ovine system using a Kelvin Model*, submitted 2007.
2. P. Bai, H.T. Banks, S. Dediu, A.Y. Govan, M. Last, A. Lloyd, H.K. Nguyen, M.S. Olufsen, G. Rempala, B.D. Slenning. *Stochastic and deterministic models for agricultural production networks*, submitted 2007.
3. B.N. Steele, M.S. Olufsen, and C.A. Taylor. *Impedance boundary condition for rest and exercise with in vivo validation*. Comp Met Biomech Biomed Eng, 10: 39-51, 2007.
4. M.S. Olufsen, H.T. Tran, J.T. Ottesen, REU program, L.A. Lipsitz, V. Novak. *Modeling baroreflex regulation of heart rate during orthostatic stress,* Am J Physiol, , 291:R1355-R1368, 2006.
5. D.H. Justice, H.J Trussell, M.S. Olufsen. *Analysis of blood flow velocity and pressure signals using the multipulse method,* Math Biosci Eng, 3(2): 419-440 2006.
6. M.S. Olufsen, J.T. Ottesen, H.T. Tran, L.M. Ellwein, L.A. Lipsitz, and V. Novak. *Blood Pressure and blood flow variation during postural change from sitting to standing - Mathematical modeling and experimental validation,* J Appl Physiol, 99:1523-1537, 2005.
7. M.S. Olufsen, H.T. Tran, and L.A. Lipsitz. *Modeling Cerebral Blood Flow Control During Posture Change fro Sitting to Standing,* J Cardiovasc Eng, 4(1): 47-58, 2004.
8. M.S. Olufsen and A. Nadim. *On deriving lumped models for blood flow and pressure in the systemic arteries*, Math Biosci Eng, 1(1): 61-80, 2004.
9. M.S. Olufsen, M.A. Whittington, M. Camperi, and N. Kopell. *New roles for the gamma rhythm: Population tuning and preprocessing,* J Comp Neurosci, 13:33-54, 2003.
10. M.S. Olufsen, A. Nadim, and L.A. Lipsitz. *Dynamics of cerebral blood flow regulation explained using a lumped parameter model.* Am J Physiol, Reg Int Comp Physiol, 282:611-622, 2002.
11. M.S. Olufsen, C.S. Peskin, W.Y. Kim, E.M. Pedersen, A. Nadim, and J. Larsen. *Numerical simulation and experimental validation of blood flow in arteries with structured-tree outflow conditions*. Ann Biomed Eng, 28(11):1281-1299, 2000.
12. M.S. Olufsen. A structured tree outflow condition for blood flow in the large systemic arteries, Am J Physiol, 276:257-268, 1999.

Books:

1. J.T. Ottesen, M.S. Olufsen, and J.K Larsen. *Mathematical Models in Human Physiology*. SIAM, Philadelphia, 2004.

Book Chapters:

1. J.K. Larsen, V. Andreasen, H. Larsen, M.S. Olufsen, J.T. Ottesen. Cardiovascular modelling at IMFUFA, in *The way through science and philosophy: Essays in honor of Stig Andur Pedersen*, H.B. Andersen, F.V. Christiansen, K.F. Jorgensen, V.F. Hendricks (editors). Tributes Volume 4, College Publications, London, pp. 87-96, 2006.
2. M.S. Olufsen. *A one-dimensional fluid dynamic model of the systemic arteries*. In Computational Modeling in Biological Fluid Dynamics, L.J. Fauchi and S. Gueron (eds), IMA Volumes in Mathematics and its Applications, 124:167-188, 2001.
3. M.S. Olufsen. *A one-dimensional fluid dynamic model of the systemic arteries*. In Mathematical modelling in medicine, Stud Health Technol Inf., J.T. Ottesen, M. Danielsen (eds), 71: 79-98, 2000.

Peer Reviewed Proceeding Articles:

1. D.H. Justice, H.J. Trussell, and M.S. Olufsen. *Using Speech Processing Methods to Model Blood Flow Signals*. Proc 13th European Signal Processing Conference, 2005.
2. D.H. Justice, H.J Trussell, and M.S. Olufsen. *Modeling of blood flow velocity and pressure signals using the multipulse method*. Proc 11th IEEE Digital Signal Processing Workshop, 320-324, 2004.

3. M.S. Olufsen and A. Nadim. *Lumped models for blood flow and pressure in the systemic arteries*. Proc 2nd MIT conf Comp Fluid and Solid Mech, K.J. Bathe (ed). Elsevier Science, 2:1786-1789, 2003.
4. M.S. Olufsen, L.A. Lipsitz, and A. Nadim. *A Lumped Parameter Model for Cerebral Blood Flow Regulation*. Advances in Bioengineering, 51:277-278, 2001.
5. M.S. Olufsen, A. Nadim, and L. Lipsitz. *Autoregulation of cerebral blood flow*. Proc IEEE 26th Ann Northeast Bioeng Conf, 41-42, 2000.
6. M.S. Olufsen and J.T. Ottesen. *Outflow conditions in human arterial flow*. In Computer simulations in biomedicine, Proc Third Int Conf Comput Simul Biomed, Biomed '95. H. Power, R.T. Hart (eds). Computational Mechanics Publications, 249-256, 1995.

PhD Thesis:
1. M.S. Olufsen. *Modeling the arterial system with reference to an anesthesia simulator*, Text 345, IMFUFA, Roskilde University, Denmark, 1998.

Masters Thesis:
1. M.S. Olufsen and O.M. Nielsen. *Disco – Discrete and continuous simulation in Turbo Pascal*. Department of Computer Science, Roskilde University, Denmark, 1993.

Research Presentations (Conferences and Workshops):
1. Workshop on Blood Flow in the Microcirculation: Function, Regulation, and Adaptation. The Mathematical Biosciences Institute (MBI), The Ohio State University, January 22-26, 2007. Invited speaker.
2. Workshop on Short-term Cardiovascular-Respiratory Control Mechanisms, sponsored by American Institute of Mathematics (AIM), October 9-13th, 2006. Main organizer.
3. Meeting in the honor of Charles Peskin's 60th Birthday, Courant Institute, NYU, Oct 20-21, 2006. Invited speaker.
4. Sarajevo Summer School: Mathematical Techniques in Modeling Physiological Systems, Sep 10-22, 2006. Invited to teach module on model analysis.
5. SIAM Conference on the Life Sciences, Raleigh, Jul 31- Aug 4, 2006. Organized minisymposium and presented a poster.
6. Pulmonary Circulation Workshop, June 7th, 2006. Invited to give a plenary presentation.
7. Experimental Biology, San Fransisco, Apr 1-5, 2006. Invited to speak at the symposium on trends in experimental pathology sponsored by Robert E. Stowell,
8. Agricultural Systems Working Group, 2005-2006 Program on National Defense an Homeland Security (NDHS), Statistical and Applied Mathematics Institute (SAMSI), Group Leader.
9. Joint meeting, Southeastern Section MAA SIAM Southeast Atlantic Section, Auburn, AL, Mar 31- Apr 1. My students E. Tweedy (undergraduate) gave a talk and won a cash award for best student presentation.
10. AMS annual meeting, Atlanta, Jan 29–Feb 2, 2006. REU students (Tweedy, Benin, Joyner, and Vogl) presented a poster and won a cash award for best student presentation.
11. BMES annual meeting, Baltimore, MD, Sep 28-Oct 1, 2005. My student E. Tweedy (undergraduate) presented a poster.
12. 13th European Signal Processing Conference (EUSIPCO), Antalya, Turkey, Sep 4-8, 2005. Presented poster in collaboration with D.H. Justice, and H.J. Trussell (presenter).
13. SIAM Annual meeting. New Orleans, LA, Jul 11-14, 2005. Organized minisymposia and presented a talk.
14. Mini-invasive procedures in medicine and surgery: Mathematical and numerical challenges. CRM Montreal, Workshop, May 23-27, 2005. Invited to present a one-hour lecture.

15. 29th Annual SIAM-SEAS Meeting, Charleston, SC, Mar 25-26, 2005. Two of my students, D. Valdez-Jasso (undergraduate student) and L.M. Ellwein (graduate student) presented their work. Laura Ellwein won a cash award for best student presentation.
16. 11th IEEE Digital Processing Workshop, Taos, New Mexico, Aug 1-4, 2004. Poster presented in collaboration with D.H. Justice and H.J. Trussell (presenter).
17. SIAM Conference on the Life Sciences, Portland, Jul 11-14, 2004. Organized minisymposium and presented a talk.
18. Redraider Minisymposium, Mathematical and computational modeling of biological systems, Texas Tech University, Nov 6-8, 2003. Outstanding early career speaker, was intived to give a one-hour lecture.
19. American Mathematical Society Fall Southestern Meeting, Chapel Hill, NC, Oct 24-25, 2003. Invited to present a talk in a minisymposium.
20. Fifth International Congress on Industrial and Applied Mathematics (ICIAM), Sydney, Australia, Jul 7-11, 2003. Organized minisymposium and presented a talk.
21. Second MIT conference on Computational Fluid and Solid Mechanics, Boston, MA, Jun17-20, 2003. Invited to present a talk in a minisymposium.
22. Fourth World congress of Biomechanics, Calgary, Canada, Aug 4-9, 2002. Presented a contributed talk and was invited to chair a session.
23. 5th Conference on Mathematical Modeling & Computing in Biology and Medicine, Milan, Italy, Jul 2-6, 2002. Invited to present a talk in a minisymposium.
24. First SIAM Meeting for Life Sciences, Boston, MA, Mar 6-8, 2002. Organized a minisymposium and presented a talk.
25. ASME international Mechanical Engineering Congress & Exposition, New York, NY, Nov 11-16, 2001. Presented a contributed talk.
26. Biomedical Engineering Society Annul Fall Meeting, Durham, NC, Nov 4-9, 2001. Invited to present two talks in minisymposia.
27. Fifth International Conference on Cognitive and Neural Systems, Boston, MA, May-Jun 31-2, 2001. Presented a contributed poster.
28. Society for Neuroscience Annual Meeting, New Orleans, LU, Nov 4-9, 2000. Presented a contributed poster.
29. IEEE 26th Annual Northeast Bioengineering Conference, University of Conneticut, Storres, CT, Apr 8-9, 2000. Invited to present a talk in a minisymposia.
30. Fourth International Congress on Industrial and Applied Mathematics (ICIAM), Edingburgh, UK, Jul 5-9, 1999. Organized a minisymposium and presented a talk.
31. Workshop on Computational Modeling in Biological Fluid Dynamics, Institute for Mathematics and its Application (IMA), Minneapolis, MI, Jan 25-29, 1999. Presented a contributed poster.
32. American Physics Society, Division of Fluid Dynamics, 51st Annual Meeting, Philadelphia, PE, Nov 22-24, 1998. Presented a contributed talk.
33. Third World Congress of Biomechanics, Sapporo, Japan, Aug 2-8, 1998. Presented a contributed talk and was invited to chair a session.
34. Cardiac Modeling Workshop, Department of Mathematics, Roskilde University, Denmark, May 18, 1998. Organized workshop.
35. First Topical Meeting on Biophysics and Biological Physics, Niels Bohr Institute, Denmark, Mar 25, 1998. Presented a contributed talk.
36. International Conference on Mathematical Modeling in Medicine, IMFUFA, Roskilde University, Denmark, Sep 25-26, 1997. Presented a contributed talk.
37. World Congress on Medical Physics and Biomedical Engineering, Nice, France, Sep 14-19, 1997. Presented a contributed talk.
38. First Workshop on Industrial Mathematics for Nordic Ph.D. students, Hillerod, Denmark, Aug 29-31, 1997. Presented a contributed talk.

39. Workshop on Bio-Medical Simulation, CRS4, Calgary, Italy, Jun 19-21, 1997. Presented an invited talk.
40. Anziam Graduate Student Day, Australian Defense Force Academy, University of New South Wales, Canberra, Australia, Oct 13, 1995. Presented a contributed talk.
41. Third International Conference for Simulations in Biomedicine, Biomed '95, Milan, Italy, Jun 21-23, 1995. Presented a contributed talk.

Seminars and Colloquia:

1. Seminar, Mathematical Biosciences Institute, The Ohio State University, OH, Feb 2006.
2. Seminar, Department of Mechanical Engineering, Imperial College, London, UK, Dec 2005.
3. Seminar, Division of Health Sciences and Technology, MIT, MA, Sep 2005.
4. Numerical Analysis Seminar, Department of Mathematics, NCSU, Aug, 2005.
5. Seminar, Department of Anesthesiology, Mayo Clinic, Jacksonville, FL, Jun 2005.
6. Special topics course in biomathematics, Department of Mathematics and Physics, Roskilde University, Denmark, Mar 2005.
7. Physics Colloquium, Dept of Physics, University of North Carolina, Wilmington, NC, Feb 2005.
8. HHMI Lecture, Meredith College, Raleigh, NC, Nov 2004.
9. AWM Seminar, Department of Mathematics, Duke University, Durham, NC, Apr 2004.
10. Seminar, Department of Mathematics and Physics, Roskilde University, Denmark, Mar 2004.
11. HHMI Lecture, Salem College, Winston Salem, NC, Dec 2004.
12. Seminar, Department of Electrical and Computer Engineering, NCSU, Raleigh, NC, Sep 2003.
13. PDE/Applied Math Seminar, Department of Mathematics, University of Houston, TX, Nov 2002.
14. Applied Mathematics Seminar, Department of Mathematics, UNC, Chapel Hill, NC, Sep 2002.
15. Seminar, Istituto per le Applicazioni del Calcolo – CNR Viale del Policlinico, Rome, Italy, Jul 2002.
16. Seminar, Keck Graduate Institute, Claremont Colleges, Claremont, CA, Jun 2002.
17. Differential Equations Seminar, Department of Mathematics, NCSU, Raleigh, NC, Nov 2001.
18. Numerical Analysis Seminar, Department of Mathematics, NCSU, Raleigh, NC, Oct 2001.
19. Neuroscience Seminar, Boston University, Boston, MA, Apr 2000.
20. Research in Progress Seminar, Research and Training Institute, Hebrew Rehabilitation Center for Aged, Boston, MA, Nov 1999.
21. Fluid Mechanics Seminar, Department of Mechanical Engineering, MIT, Cambridge MA, Nov 1999.
22. Center for BioDynamics Seminar, Dept of Mathematics, Boston University, Boston, MA, Feb 1999.
23. Brown Bag Seminar, Department of Aerospace and Mechanical Engineering, Boston University, Boston, MA, Jan 1999.
24. Graduate Student Seminar, Department of Mathematics, Duke University, Durham, NC, Apr 1998.
25. Mathematics Seminar, Department of Mathematics, Australian Defense Force Academy, University of New South Wales, Canberra, Australia, Aug 1995.

Other workshops:

Mathematical modeling workshops at NCSU, 2004-2006 co-organizer, 2002, 2004-2006 faculty mentor.

Honors and Awards:

1. Outstanding Early Career Speaker, Redraider Minisymposium. *Mathematical and computational modeling of biological systems*, Texas Tech University, Nov 6-8, 2003.
2. Society for Industrial and Applied Mathematics (SIAM): Travel award for *International Congress on Industrial and Applied Mathematics, ICIAM*, Edinburgh, UK, Jul 5-9, 1999.
3. Traveling Fellowship for Mathematicians, a Danish fellowship covering all expenses for one year of studies abroad. The fellowship was awarded with O.M. Nielsen, Urban Risk Research Group, Geoscience, Canberra, Australia, Jul 1995- Jul 1996.
4. Danish Academy of Technical Science Fellowship (EF# 501), 1994-1998.

Graduate Students at NCSU:
1. Daniela Valdez, PhD student, expected graduation May 2010.
2. April Allston, PhD student, expected graduation May 2010.
3. Laura M. Ellwein, PhD student, expected graduation May 2008.
4. Anna Hart, MS student, expected graduation Feb 2007.
5. Anjela Govan, PhD student, SAMSI program academic year 2005-2006.
6. Cynthia Chmielewski, MS in Biomathematics, graduated Aug 2003.
   Currently PhD student in Department of Mathematics, University of Houston.

Undergraduate Students at NCSU:
1. Derek Justice, B.S. Electrical Engineering, graduated May 2003.
2. David Hysom, B.S. Mathematics, graduated Dec 2003.
3. Mark Harris, B.S. Mathematics and Physics, graduated May 2004.
4. Daniela Valdez, Mathematics, graduated May 2005.
5. David Robinson, Mathematics and Statistics, expected graduation (BS/MS) May 2006.
6. Robert Benin, Mathematics, The University of Portland, WA, REU summer 2005, expected graduation May 2007.
7. Sarah Joyner, Mathematics, Meredith College, Raleigh, NC, REU summer 2005, graduated May 2006, admitted to NCSU PhD program in mathematics.
8. Eamonn Tweedy, Mathematics, REU summer 2005 and academic year 2005-2006, graduated May 2006. Admitted to UCLA's PhD program in mathematics.
9. Chris Vogl, Mathematics, REU summer 2005, graduated May 2006. Admitted to UCLA's PhD program in mathematics.
10. Cheryl Zapata, Mathematics, REU summer 2006 and academic year 2006-2007, expected graduation May 2008.
11. Kelly Koser, Mathematics Carnegie Mellon, REU summer 2006, expected graduation May 2008.
12. Julia Moore, Mathematics RPI, REU summer 2006, expected graduation May 2007.

Editorial Responsibilities:
Mathematical Biosciences and Engineering. Associate editor 2007-2010.

Refereed journal articles for: SIAM journal of Applied Mathematics, SIAM Journal of Dynamical Systems, Journal of Fluid Mechanics, Journal of Mathematical Biology, The Journal of General Physiology, IEEE Transactions of Biomedical Engineering, Journal of Computational Neuroscience, Physica D, Proceedings for the National Academy of Sciences, Mathematical Models and Methods in Applied Sciences, Journal of Autonomic Neuroscience: Basic and Clinical.

Refereed research proposals for the National Institute of Health (both as an ad-hoc member of a review panel and as a mail in reviewer) and for the National Science Foundation (as a mail in reviewer).

Mentors and Collaborators:
PhD Advisors and Mentors

<u>Stig Andur Pedersen (PhD), Professor (academic advisor)</u>
Department of Philosophy and Science Studies
Roskilde University, PA6, 4000 Roskilde, Denmark
Email: **sap@ruc.dk**
Phone: +45 4674 2265

<u>Jesper Larsen (PhD), Director (industrial advisor)</u>
Math-Tech
Ordurphojvej 54, 1st, 2920 Charlottenlund, Denmark

Email: **jesper@math-tech.dk**
Phone: +45 3315 3309

Charles Peskin (PhD), Professor (mentor)
Department of Mathematical Sciences
New York University, NY
Email: **peskin@cims.nyu.edu**
Phone: 212 998 3126

Postdoc Mentors

Ali Nadim (PhD), Professor
Keck Graduate Institute
535 Watson Drive, Claremont, CA 91711
Email: **nadim@kgi.edu**
Phone: 909 607 9650

Nancy Kopell (PhD), Professor
Department of Mathematics
Boston University
111 Cummington Street, Boston, MA 02215
Email: **nk@math.bu.edu**
Phone: 617 353 5210

Collaborators

Hien Tran (PhD), Professor
Department of Mathematics
North Carolina State University
Campus Box 8205, Raleigh, NC 27695
Email: **tran@math.ncsu.edu**
Phone: 919 515 8782

Pierre Gremaud (PhD), Professor
Department of Mathematics
North Carolina State University
Campus Box 8205, Raleigh, NC 27695
Email: **gremaud@math.ncsu.edu**
Phone: 919 515 3085

Tim Kelley (PhD), Professor
Department of Mathematics
North Carolina State University
Campus Box 8205, Raleigh, NC 27695
Email: **tim_kelley@ncsu.edu**
Phone: 919 515 7163

Mansoor Haider (PhD), Associate Professor
Department of Mathematics
North Carolina State University
Campus Box 8205, Raleigh, NC 27695
Email: **mahaider@math.ncsu.edu**
Phone: 919 515 3100

Joell Trussell (PhD), Professor
Department of Electrical and Computer Engineering
North Carolina State University
Campus Box 7911, Raleigh, NC 27695
Email: **hjt@ncsu.edu**
Phone: 919 515 5091

Brooke Steele (PhD), Assistant Professor
Department of Biomedical Engineering
North Carolina State University
Campus Box 7115, Raleigh, NC 27695
Email: **bnsteele@bme.ncsu.edu**
Phone: 919 513 8231

Johnny Ottesen (PhD), Associate Professor
Department of Mathematics and Physics
Roskilde University
Universitetsvej 1, Box 260, 4000 Roskilde, Denmark
Email: **johnny@mmf.ruc.dk**
Phone: +45 4674 2298

Vera Novak (PhD), Assistant Professor
Division of Gerontology
Beth Israel Deaconess Medical Center and Harvard Medical School
110 Francis Street, Boston, MA 02215
Email: **vnovak@bidmc.harvard.edu**
Phone: 617 632 8680

Lewis Lipsitz (MD), Professor
Chief
Division of Gerontology
Beth Israel Deaconess Medical Center and Harvard Medical School
110 Francis Street, Boston, MA 02215
Email: **llipsitz@bidmc.harvard.edu**
Phone: 617 632 8696

Vice president for academic medicine
Hebrew SeniorLife
1200 Centre Street, Boston, MA 02131
Email: **lipsitz@mail.hrca.harvard.edu**
Phone: 617 363 8318

Daniel Bia Santana (MD/PhD), Professor
Cardiovascular Research, Physiology Department
Faculty of Medicine
Universidad de la Republica
General Flores 2125, PC: 11800
Montevideo, Uruguay, South America
Email: dbia@fmed.edu.uy
Phone: +598 2 9243414 (3313)

PART II: Research Experience

My research experience is in the fields of biofluid dynamics, mathematical modeling, and interdisciplinary research in areas of cardiovascular physiology and computational neuroscience. In particular, I have studied short-term cardiovascular regulation and dynamics of blood flow and pressure as well as the activity of networks of neurons in the hippocamus; see detailed description below. My work involves aspects of engineering, mathematics, physiology, and biology. To include all aspects, I find it important to collaborate with experts from all of these disciplines.

Modeling Cardiovascular Regulation

Syncope (fainting) accounts for significant morbidity and mortality in elderly people, but it is difficult to predict. Syncope occurs as a response to oxygen (O_2) depletion due to sudden declines in cerebral (brain) blood flow. It may be caused by volume redistribution due to changes in peripheral vascular resistances, reduced blood volume, or irregular heart rhythms. Cerebral blood flow may also fall during hyperventilation, which commonly precedes syncope. However, hyperventilation increases the O_2 concentration while reducing the concentration of carbon dioxide (CO_2). As a result, the normal response to hyperventilation is cerebral vasoconstriction, which further reduce cerebral blood flow. On the other hand, CO_2 rebreathing increases cerebral blood flow. Consequently, it has been suggested that CO_2 rebreathing may prevent syncope. Under normal conditions, cerebral regulatory mechanisms maintain cerebral perfusion, and as a result, syncope is avoided. In conclusion, syncope may be a response to alterations in cerebral blood flow regulation.

The system described above involves complex interactions among various mechanisms that play a role in short-term cardiovascular and respiratory regulation. Typically, the regulatory capacity is studied based on non-invasive techniques, which limits the information that can be monitored. Typical parameters that are monitored include heart rate, ECG, blood flow velocity, finger blood pressure, inspiratory and expiratory concentration of CO_2 and O_2. These quantities describe the state of the system, and how dynamics influence the system under various conditions, e.g., during head-up-tilt, lower-body-negative-pressure, or postural change from sitting to standing. However, people affiliated with the medical community is not directly interested in the quantities that are measured but how underlying parameters such as vessel resistance or vessel tone changes. Consequently, this problem can be viewed as a complex inverse problem, where the outputs are known and limited information is available about the mechanisms that give rise to the observed quantities.

In my research on short-term cardiovascular regulation, I have used mathematical modeling to put forward hypotheses that may explain dynamics leading to observed output parameters. In recent work I have developed a mathematical model that can describe changes in cerebral blood flow velocity and finger arterial pressure during postural change from sitting to standing. This model, see [2,3], uses an electrical analog model to describe the flow and pressure of the cardiovascular system. The short-term regulation is modeled by letting parameters in the circuit (e.g., resistances, capacitors, or heart parameters) change following relations that can be justified based on the biology. Flow and pressure in the basic circuit is described by a system of linear first order differential equations combined with a non-linear forcing function that describe the beating of the heart. To respond to postural change hydrostatic effects are accounted for by introduction of a gravity model. To account for short-term regulation parameters in the circuit are modeled using non-linear set-point differential equations [2,3]. Initial values for all parameters are obtained from standard physiological observations. However, all people are different, hence standard initial values do not describe a specific dynamic observations for individual subjects. Hence, to validate our mathematical model we have used non-linear optimization to estimate individual parameters for a given subject. Furthermore, we developed a detailed model that predicts baroreflex regulation of heart rate during postural change from sitting to standing [1]. With this model we were able to develop new quantities that can be used to differentiate between young, healthy elderly, and hypertensive elderly people. This model was validated against 60 datasets, 20 datasets from each group.

In future work, my main goal is to develop and analyze more comprehensive models that can predict short-term interactions between cardiovascular and respiratory systems and their effects on cerebral chemo- and pressure regulation in the supine position and during orthostatic stress. In particular, I plan to use mathematical models to explore the cardio-respiratory interactions based on responses observed during experimental protocols for hyperventilation and carbon dioxide (CO_2) rebreathing in the supine position. To reach this goal, we plan to further develop the mathematical model described [1, 2, 3]. In particular I plan to develop three sub-models: (i) A cardiovascular model that can predict arterial blood pressure, cerebral and radial blood flow velocity (BFV), (ii) a model that can predict sympathetic and parasympathetic activity of the autonomic nervous system during adaptation to orthostatic stress, and (iii) a model that can predict concentrations of CO_2 and oxygen (O_2) in the expiratory air. These three models will be combined to determine their interactions and contributions to cerebral perfusion. I plan to validate this mathematical model against measured data from young and old normotensive subjects during hyperventilation and CO_2 rebreathing in supine position and during head-up-tilt (including normotensive subjects who fainted during head-up-tilt). The mathematical model that I plan to develop has potential to help obtain a better understanding of the mechanisms involved in the interaction between the cardiovascular and respiratory control during orthostatic stress. This research project will involve a new approach to better understand cardiovascular and respiratory control systems influencing cerebral blood flow.

An important part of this research will be to evaluate the strength of the physiological evidence supporting postulated mechanisms. In particular, we plan to estimate model parameters and to perform formal sensitivity analysis. In parameter estimation, error functions quantify the discrepancy between experimentally measured and analytical/model predicted response data. Sensitivity analyses are performed to evaluate the gradients of the error functions with respect to the model parameters. The sensitivities are then used to modify the model parameters to correlate the predicted model and experimental response data. Sensitivity information is also valuable in its own right. Sensitivity analysis plays a critical role in the process of validation for a complex model. It is important to determine for which parameters a model is very sensitive. This may reflect a property of the real system, but may also be the result of shortcomings of the model. Determining these parameters against which the model is very sensitive is very important when it comes to adapt a model to individual persons. On the other hand, parameters, which do not influence the behavior of the model significantly, can be determined roughly as averages from sufficiently large samples. This could reduce the dimensionality of the underlying parameter identification problem considerably.

This project will be carried out in collaboration with members of the “Research Group on Heart-Brain Control Systems”. Members of this group include Dr. Hien Tran, NCSU, Dr. Jerry Batzel and Dr. Franz Kappel, Institute for Mathematics, University of Graz, Dr. Vera Novak and Dr. Lew Lipsitz, Beth Israel Deaconess Medical Center, Boston, and Dr. Johnny Ottesen, Department of Mathematics, Roskilde University, Denmark.

The model approach discussed above can be used to study a large range of cardiovascular problems such as aging, diabetes, stroke, and control of left ventricular assist devices. It is my aim to develop a basic model paradigm that can be used for all pathologies. For example to study control of left ventricular assist devices, it will be necessary to develop a more detailed heart model or possibly to let some of the parameters represent physiological states, while the basic circulatory model may remain unchanged.

Analysis of Blood Flow Regulation Data using Signal Processing

In collaboration with Dr. H.J. Trussell, Department of Electrical and Computer Engineering at NCSU, I have worked on another project trying to describe trends in blood pressure regulation data discussed above. In this project we used digital signal processing methods to analyze datasets for group of subjects of healthy young, healthy and hypertensive elderly people. In this work we showed that signals for finger blood pressure and cerebral blood flow velocity can be analyzed independently of each other using the multipulse method, which was developed to analyze speech signals [10-12]. Our method produces a sequence of input impulses while at the same time computing an AR model. This allows us to model the signal at high resolution between beats. Because of this, we can track the changes of the vascular system on a much finer time scale than previous methods. Furthermore, the use of an AR model permits interpretation by the use of other derived system parameters such as reflection coefficients, tube radii, poles and zeros. With this method we have been able to accurately predict dynamics of flow and pressure waveforms. In particular our method has revealed that representation of model parameters in the form of a collection of tube radii reveals significant differences between the group of young people versus the groups of healthy and hypertensive elderly people. Currently we are working on developing statistical measures to quantify these differences and from these provide physiological interpretations of our results.

Modeling Cardiovascular Dynamics

Blood flow in the systemic arteries is essentially three-dimensional, hence to obtain accurate predictions the complete Navier-Stokes equations should be solved. However, three-dimensional models require immense computational resources to be solved accurately. For questions involving large systems this is not feasible. For such systems one-dimensional models form an excellent alternative to three-dimensional analysis. The one-dimensional equations can be solved significantly faster than the three-dimensional equations.

My work on modeling dynamics of arterial blood flow [4-8] concerned development and validation of a mathematical model that can predict the time dependent flow and pressure at any location in the human systemic arteries. The model is based on a fluid dynamic approach, solving the one-dimensional Navier-Stokes equations combined with a constitutive equation that relates pressure to the cross-sectional area. This constitutive equation was obtained using linear elasticity theory combined with experimental knowledge on arterial compliance. Equations were solved for all large vessels in the systemic arterial tree. Each of the vessels (each branch in the tree) was modeled as an elastic and tapering vessel. An important aspect of the project was to develop a physiologically outflow boundary condition allowing the arterial tree to be truncated after a few generations. The boundary condition comprised an asymmetric structured tree in which at each generation the radii of the daughter vessels were scaled linearly from the radius of the parent vessel. Using this structured tree model made it possible to reduce the computational work, while retaining essential properties of the full arterial tree. Each of the small arteries in the structured tree was modeled as an elastic vessel in which the linearized viscous Navier-Stokes equations were solved. The boundary condition attached at the outflow of the large arteries was then determined from the impedance computed at the root of this structured trees.

At first this model was validated against one dataset obtained in collaboration with Drs. E.M. Pedersen and W.Y. Kim, Skejby University Hospital, Denmark. This model validation was performed by measuring blood pressure in the arm as well as at 10 specific locations along the major systemic arteries. Our study showed an excellent agreement between the measurements and the simulations [5]. More recently, the model has been validated against both rest and exercise data [8]. Simulations for both rest and exercise displayed excellent agreement with data.

However, many shortfalls must be addressed before one-dimensional models can be used for practical purposes. For example, if the model is to be used for surgery planning, it is important to develop efficient methods to reconstruct geometrical interfaces. Furthermore, a more accurate constitutive equation that describes the viscoelastic properties of arteries must be included, and equations that describe the loss of energy over bifurcations or bypasses must be developed. Recently, I have established collaboration with Dr. Bia, Physiology Department, Universidad de la Republica, Uruguay, who have used in-vitro methods to simultaneously measure blood pressure and cross-sectional area. In collaboration with Dr. Haider, Mathemematics, NCSU, we are currently working on developing and validating viscoelastic models that can describe the pressure area-relationships.

Flow in the arterial network is three-dimensional and at junctions vortices are formed, which gives rise to loss of energy. To model the entire or even large parts of the arterial network in 3D is not feasible due to the size of the domain. Our preliminary work [4-8] has shown that it is feasible to use a one-dimensional model that includes loss terms that describe the net effect of these vortices. In previous work cited above we used a steady-state approximation, which is not correct, since arterial blood flow is unsteady. To improve the models it is my plan to pursue some of these problems in more details.

One application of this model that I plan to pursue in the near future is to study changes in waveforms in the brain. As the pulse-wave travels towards the periphery part of the wave is transmitted, while part of the wave is reflected. The degree of wave-reflection depends on the resistance of the peripheral vascular bed distal to the artery in question, as well as on the specific geometry of the network. As described above, resistances of the vascular bed are regulated, changing under various physiological conditions. To account for these changes, it is important to be able to continuously change the outflow boundary conditions. Furthermore, to account for the specific geometry, it is important to be able to accurately predict pressure losses that occur at branches. It is known that waveforms recorded in the brain differ during different conditions. It is our goal to use the one-dimensional fluid dynamics model to evaluate variations in waveforms under different physiological conditions. This work will be carried out in collaboration with Dr. Gremaud, Mathematics, NCSU and Dr. Novak, Beth Israel Deaconess Medical Center, Boston.

Computational Neuroscience

During my postdoc at Boston University, I worked on modeling activity in networks of neurons in collaboration with Dr. Nancy Kopell. In particular we studied the dynamics of gamma (30-80 Hz) and beta (12-30 Hz) rhythms and their role in creation and modulation of cell-assemblies (subsets of cells that fire synchronously) [9]. Such phenomena can be found in the hippocampus, the part of the brain thought to be associated with memory formation. Cell-assemblies are also important in the visual system, during figure-ground separation. We tried to understand how cell-assemblies can be formed and modulated using networks of neurons in which spiking activity is obtained using the Hodgkin-Huxley equations. The networks we studied contained excitatory pyramidal cells and inhibitory interneurons, each with an applied current, a leak current, and a number of spiking currents. In addition, the cells are synaptically coupled. We showed that creation and modulation of the cell-assemblies are strongly dependent on a number of factors: The strength of the coupling, the specific routes for the coupling, and plastic changes of connections during transitions from the fast gamma rhythm to the slower beta rhythm. In addition we focused on dynamics of the applied current. Our results are based on simulations and we have studied the effects of changing the model parameters and cell connectivity, as well as understanding the different levels of timing of interspike-intervals. Besides our modeling efforts we found it important to validate our findings and thus we worked with Dr. Miles Whittington (University of Leeds) who tested our hypotheses in hippocampal slices.

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PART III: Teaching Experience

I enjoy teaching and find it very important to treat the students with respect and involve them actively in lectures. I try to encourage students who fall behind by sending them personal emails and schedule meetings with them to discuss how they best can catch up on missing lectures. I discovered that encouraging students to ask questions as well as assigning small exercises for in class expositions by the students resulted in a lively dialog and helped to motivate the students.

At North Carolina state university I have taught classes ranging from introductory calculus for incoming freshmen to advanced graduate courses in fluid mechanics. MA131 is the first course in a two-semester calculus sequence for non-math and non-engineering majors. Most students in MA131 are biology students, pre-vet students or pre-med students. These are students who often have weak mathematical intuition. To motivate students in MA131 I often use examples from my research and spend time explaining how they may use concepts in calculus at later stages of their education and career. MA241 and MA242 are two courses in a three-semester calculus sequence for engineering students. MA325 is an introduction to mathematical modeling for freshmen and sophomore students. This course consists of five modules each taught by different people. Spring 2005 I have taught one module (three weeks), introducing mathematical modeling of the cardiovascular system. MA341 is an introduction to differential equations. This course mainly attracts students from mathematics and engineering. MA432 is a required modeling course for math-majors. Our department offers two such courses, one with emphasis on physics and one with an emphasis on biological sciences. I taught the course with emphasis on biological sciences twice, the main focus of this course has been to provide students with examples of how mathematical models can be used in biological sciences. One of the main criteria for this course has been to have students work on mini-projects in groups of 3-4 students. MA591 is a mathematical modeling course for graduate students in mathematics and biological sciences. The idea with this course is to team up students who have a biological background with students who have a mathematical background. After introducing concepts of modeling, these teams of students have to develop models on their own based on research projects of interest to the team. For example, one group worked on modeling nitrogen uptake in corn, while another group worked on the life cycle needed to maintain a fishery. Finally, MA797 is a graduate level special topics course in fluid dynamics. In the spring 2005, this course was taught using videoconferencing enabling biomedical engineering students located at the university of North Carolina, Chapel Hill Campus to participate in the course.

In addition to traditional classroom teaching I have three times been involved with a mathematical modeling workshop that lasts for 10 days. During this workshop investigators from industry propose problems that groups of students try to analyze. I was working on mentoring the students together with the problem presenter from industry. In addition, I have been advising a group of REU (research experience for undergraduate students) summers 2005 and 2006. This effort was during the first year that NCSU mathematics started the REU program. The students worked during 10 weeks under my supervision to solve a problem related to my research. Results from summer 2005 have been accepted for publication [1] and students participating in this work won 4 cash research awards at regional and national meetings. We anticipate to write up publications based on results obtained during the summer 2006.

At Boston University, I team-taught a course in introductory physiology in department of biomedical engineering. I was teaching the part on cardiovascular physiology.

At Roskilde University, I taught introductory calculus, introductory object oriented programming, and I team-taught a special topics course in fluid dynamics. In addition I supervised 4 student projects. At Roskilde University, the teaching is based on problem-based learning. Each semester all students are supposed to work in teams of 3-4 to develop a project. I supervised such projects both for undergraduate students and for graduate students pursuing a Masters degree.

I incorporate technology into my teaching by using computers when appropriate to demonstrate connections and to facilitate better communication among students. When supervising projects in applied mathematics I find it important to teach the mathematical background needed as well as to keep the interdisciplinary problem in focus.

Teaching Experience at NCSU:

Classes:

Fall 2006	MA131	Analytic geometry and calculus A (2 sections w/ 100 students)
Spring 2006	MA432	Mathematical models in life and social sciences (15 students)
	MA591	Special topics in differential equations II (10 students)
	MA325	An introduction to applied mathematics (35 students)
Fall2005	MA341	Differential equations (30 students)
Spring 2005	MA797	BioFluid dynamics (6 students)
	MA591	Special topics in differential equations II (10 students)
	MA325	An introduction to applied mathematics (40 students)
Fall 2004	MA131	Analytic geometry and calculus A (100 students)
Summer 2004	MA242	Analytical geometry and calculus III (30 students)
	MA341	Differential equations (30 students)
Spring 2003	MA432	Mathematical models in life and social sciences (20 students)
	MA591	Special topics in differential equations II (10 students)
Fall 2003	MA131	Analytic geometry and calculus A (2 sections w/ 100 students)
Spring 2003	MA432	Mathematical models in life and social sciences (20 students)
Fall 2002	MA797	BioFluid dynamics (5 students)
Spring 2002	MA241H	Analytic geometry and calculus II (35 students, honors section).
Fall 2001	MA242	Analytic geometry and calculus III (35 students)

Other:

Summer 2006	Research experience for undergraduate students, I mentored one of 7 REU groups. My group was on biomathematics, the students worked on modeling cerebral autoregulation (3 students).
Summer 2006	Faculty mentor and co-organizer of the NCSU modeling workshop (6-8 students).
Summer 2005	Research experience for undergraduate students, I mentored one of two REU groups. My group was on biomathematics, the students worked on modeling heart-rate regulation (4 students).
Summer 2005	Faculty mentor and co-organizer of the NCSU modeling workshop (6-8 students).
Summer 2004	Faculty mentor for the NCSU modeling workshop (6 students).
Summer 2002	Faculty mentor for the NCSU modeling workshop (6 students).

Teaching Experience at Boston University:

Spring	2001	Introduction to Physiology, Department of Biomedical Engineering (20 students)

Teaching Experience at Roskilde University, Denmark:

Fall	1990	Introduction to object oriented programming using simula (TA), (40 students)
Spring	1991	Introduction to object oriented programming using simula (40 students)
Fall	1991	Analytical geometry and calculus 1 (TA), (100 students)
Spring	1992	Analytical geometry and calculus 2 (TA), (100 students)
Fall	1992	Analytical geometry and calculus 1 (100 students)
Spring	1993	Analytical geometry and calculus 2 (100 students)
Spring	1998	BioFluid dynamics (10 students)
1994-1997		Mentored 4 student projects each lasting one semester (4 students per project)