

NSR is funded by
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*Simulation Resource
in Circulatory Mass
Transport and
Exchange*

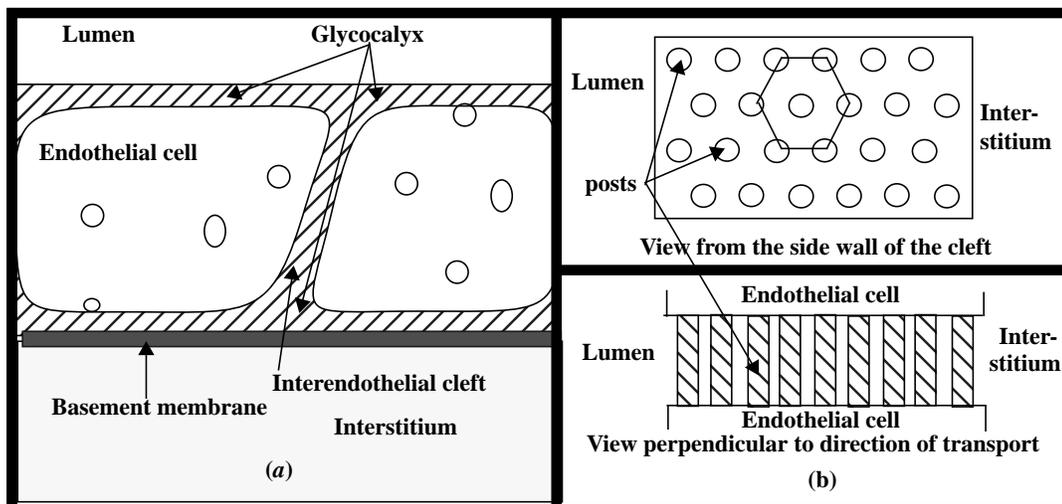
Charge effects in the Exchange of Ionized Solutes Through Interendothelial Clefts

Dana Haselton's Ph.D. thesis, completed in January, 1995, pioneers an advancement in the field of molecular hydrodynamics. The topic of solute transport through pores has been worked on all this century. See Lamb (*Hydrodynamics*: Dover, 1945), Pappenheimer (*Physiol. Rev.* 33: 387-423, 1953), Bean (in *Membranes, Vol. 1—Macroscopic Systems and Models*, ed. G. Eisenman: Dekker, 1-52, 1972), Lightfoot et al. (*Ann. Biomed. Eng.* 4: 78-90, 1976), and the review by Curry (in *Handbook of Physiology, Section 2, Volume 4*, eds. E.M. Renkin and C.C. Michel: American Physiological Society, 309-374, 1984). The previous workers understood that charge could be important because the clefts between endothelial cells in "closed" capillaries are narrow, about 15 nm, and the potential fields from the cell surfaces and from the glycocalyx extend throughout the cleft. The idealized cleft is shown in Figure 1, and the idea of the electrical double layer is shown in Figure 2. The abstract of the thesis, formally titled *Calculation of the Electrostatic Potential in an Idealized Model of Transcapillary Exchange*, is as follows:

An idealized continuum model of electrokinetic transport is developed to analyze the con-

tributions of solute and barrier charge to microvascular permeability. The glycocalyx fiber-matrix-filled interendothelial cleft of the transcapillary exchange barrier is modelled with parallel plates representing endothelial cell surfaces and a bridging regular array of identical cylinders representing glycocalyx fibers. To calculate the electrostatic potential within the confined fiber-matrix, the linear Poisson-Boltzmann equation is solved for a single bounded post and a regular array of bounded posts using several analytical methods (separation of variables, Green's functions and linear superposition and unit cell approximations) and numerical methods (direct formulation of a boundary element method and boundary collocation method). The potential decays monotonically with distance from the surfaces vanishing between four and five Debye lengths. For values typical of plasma ultrafiltrate in a glycocalyx filled interendothelial cleft, namely a Debye length of 8 Å, plate separation of 120 Å, post radius of 6 Å and surface potential of 60 mV, the potential remains nonzero for porosity values less than 97%. Thus, throughout the confined matrix region of this idealized model, there is enhanced anionic and diminished cationic convective transport

Figure 1



Contents

Charge effects in the Exchange of Ionized Solutes Through Interendothelial Clefts....	1
XSIM Status....	2
Jim Revkin: User profile....	2
Anonymous ftp at NSR....	3
NSR Experimental Biology and Microcirculatory Society Posters and Presentations....	3
World Wide Web and NSR....	4

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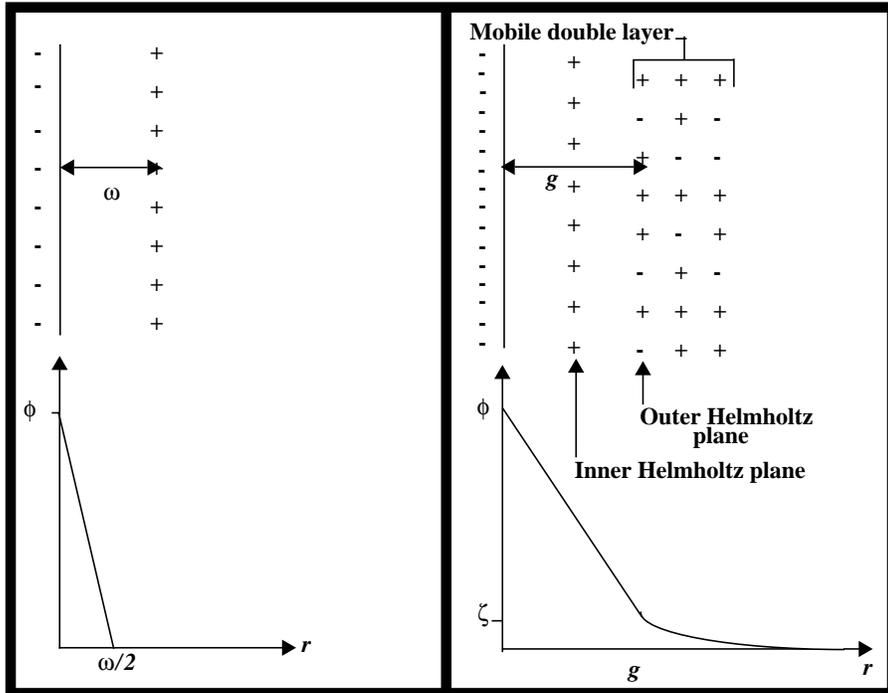
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compared to neutral molecules. The effect is more pronounced for larger molecules with double layers that extend into double layer regions close to the post or plates where the potential magnitude is greatest. This result agrees with published experimental observations of transport of charged molecules.

—Jim Bassingthwaite



Figure 2



XSIM Status

In previous issues we described XSIM, a simulation interface for use by biomedical investigators doing computer simulation. XSIM runs in a windowing environment on engineering workstations and uses the “point and click” approach that has become popular with modern computer users. An important feature of XSIM is that the appearance of the screen is not pre-defined but is determined at run time by reading a configuration file selected by the investigator. This allows the interface to be tailored to the specific analysis task at hand including a graphical depiction of the model being run. The content and appearance of pop-up windows related to the model and its parameters are also specified in the configuration file. Since the interface and model run as separate tasks, the investigator can shift to different models without leaving the interface. It also permits models to be run on remote computers when the computational demands of the model are too heavy for the local workstation. Other capabilities include parameter optimizers to fit model output to experimental data, analysis of sensitivity and residual functions, graphical display of data, and

an expression parser that enables the investigator to define new variables at run time. The first implementation of XSIM is on Sun SPARC stations using Motif™, but its design facilitates portability to other hardware platforms and window systems.

As planned, a preliminary version of XSIM was made available to selected users for evaluation on 1JAN95. Their feedback has resulted in a number of changes and improvements.

We will have a functioning version of XSIM on display at Experimental Biology 95. This version has all the control, optimization, and reporting features found in SIMCON plus a wide assortment of new features available only in XSIM. We plan thorough extensive testing and documentation of this version of XSIM before releasing it to users on 5 June.

—Rick King



Jim Revkin: User Profile

In 1985, Jim Revkin joined the Simulation Resource Facility as a Post-Doctoral Fellow. He'd completed a fellowship in Cardiovascular Disease at Yale University. At Yale, he'd done work in myocardial metabolism, studying *in vivo* myocardial substrate use in canines and human subjects. Those studies involved coronary sinus catheterization and evaluated glucose, free fatty acid, lactic acid, and amino acid flux.

At the Simulation Research Facility, Dr. Revkin was introduced to a variety of new concepts and techniques including (1) general principles behind the mathematical modeling of biologic processes, (2) the multiple indicator dilution technique as applied to isolated heart preparations, (3) myocardial PET imaging, (4) computer operations in new environments including the UNIX operating system and networking.

Dr. Revkin applied these techniques to his prior interest in myocardial protein turnover, using the multiple indicator dilution technique to evaluate radiolabeled phenylalanine flux in isolated rabbit heart preparations.

After his postdoctoral research year, Dr. Revkin joined the faculty at the University of Washington Medical School as Assistant Professor, and Medical Director of the Transplant Cardiology Program. Two years later (because he had the only grandchild on both sides of the family 2800 miles from the grandparents) he returned to Yale University, to direct their Transplant Cardiology Program.

Upon his return to Yale, he set up the SIMCON and MMID4 applications on a networked Sun Workstation and has maintained “electronic” and “spiritual” links with members of the NSR who have always been eager to support his efforts. His long-term goal is to apply

the multiple indicator dilution techniques to evaluate adenosine flux in transplanted hearts, assessing the hypothesis that adenosine flux may be altered in the rejecting allograft of patients with allograft "vasculopathy" (transplant coronary artery disease) which is now the number one cause of late transplant failure.

Dr. Revkin says "I would recommend the NSR Modeling Course or even a post-doctoral or sabbatical year to anyone interested in myocardial metabolism, blood flow, or the mathematical modeling of biological processes. There is a very high level of critical and imaginative thinking that one is exposed to. The environment invariably leads one to look at things in a new light, with often unexpected beneficial spin-offs."

—Rita Jensen



NSR at the 1995 Microcirculatory Society and Experimental Biology Meetings

NSR and several Simulation Resources, along with providers of software for teaching, will have an exhibit titled "Computer-based Resources in Teaching" in booths 606–809 at the 1995 Experimental Biology meeting. XSIM, SIMCON and other NSR software will be demonstrated on a Sun™ workstation.

Lectures, posters and presentations from individual NSR workers at the meetings are listed below with their titles, board numbers, abstract numbers, times, and locations.

Jim Bassingthwaighte

"In Vivo Biochemistry of Endothelial Cells in the Heart." Landis Award Lecture, Georgia World Congress Center, 4:30–5:30 p.m., Sunday, April 9.

"Diffusional facilitation with slow binding to protein: albumin-palmitate solutions." E. Barta, S. Sideman, J. Bassingthwaighte. Board #59, abstract #116. Saturday afternoon.

Dan Beard

"Continuum model for dispersion of a tracer with a complex microvascular arrangement." D. Beard, J.B. Bassingthwaighte. Board #119, abstract #176. Saturday afternoon.

Dana Haselton

"Calculation of the electrostatic potential in the interendothelial cleft." D.J. Haselton, S. Kim, J.B. Bassingthwaighte. Board #64, abstract #036. Saturday afternoon.

Rick King

"A graphical user interface for computer simulation." R. King. Board #A-13, abstract #11097. 8:00 a.m. Monday.

Keith Kroll

"Capillary endothelial cell adenosine transport in guinea pig heart." K. Kroll, J. Bassingthwaighte. Board #72, abstract #119. Saturday afternoon.

"PCr recovery during underperfusion in rabbit heart." K. Kroll, D.J. Kinzie, R. Gronka, M.J. Kushmerick. Abstract #11455. Oral presentation in Congress Center room 266/267, 10:15 a.m. Thursday.

Zheng Li

"Nonlinear model for oxygen metabolism using 0-15 Oxygen and PET." Z. Li, J. Bassingthwaighte. Board #44, abstract #026. Saturday morning.

Peter Tonellato

"Fractal characteristics of hemodynamic time series of a hypertensive rat population." P.J. Tonellato, A.W. Cowley, A.S. Greene, G.M. Raymond, J.B. Bassingthwaighte. Board #116, abstract #173. Saturday afternoon.

Tada Yipintsoi

"Redistribution of canine myocardial blood flow with catecholamines and adenosine." T. Yipintsoi, Z. Li, K. Kroll, E.O. Feigl, J. Ploger, J.B. Bassingthwaighte. Board #31, abstract #098. Saturday afternoon.

Anonymous ftp at NSR

You may get files from NSR by using anonymous ftp. If you are using a UNIX system, use the following steps to get the "Readme" file first, then read it carefully for detailed instructions. Macintosh and PC users may use similar procedures specific to their system and communication software.

1. Enter `ftp nsr.bioeng.washington.edu` at the system prompt.
2. Enter `anonymous` at the resulting prompt, Name:
3. Enter a complete electronic mail address at the prompt, Password:
4. Enter `get Readme` at the prompt, `ftp>`.
5. Enter `quit` to return to your system.

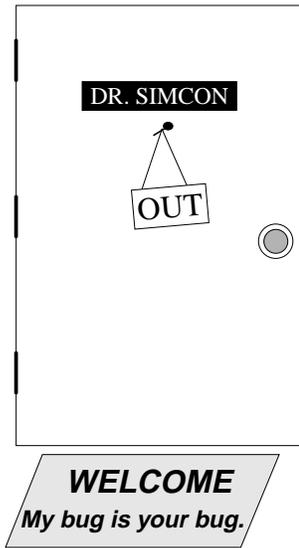
The "Readme" file is a text file that can be read with your usual text editor (e.g., vi) or word processing application.

World Wide Web and NSR

NSR has a World Wide Web (W3) home page at the Uniform Resource Locator (URL) address: <http://nsr.bioeng.washington.edu>. For the nonce, you can use Mosaic© or your favored W3 browser to access the NSR User Guide at our site: development of the site continues, however, so tune in from time to time for more goodies. While you're there, check out the link to the home page of the *Annals of Biomedical Engineering*, where you will find the tables of contents for previous and forthcoming issues of the journal, as well as information for authors. To go directly to the *Annals* home page, use the URL <http://biorobotics.ee.washington.edu/ABME/annals.html>.

COMPUTER SIMULATION SUMMER WORKSHOP SEPTEMBER 17-22, 1995

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