THE BIOLOGICAL PHYSICIST

The Newsletter of the Division of Biological Physics of the American Physical Society

Vol. 1 № 1 June 2001

In the Inaugural Issue

Dear DBP Members:

I am pleased to present you with the revamped DBP newsletter, *The Biological Physicist*, and to introduce the editor of the newsletter, Dr. Sonya Bahar, of the University of Missouri at St. Louis. This is the first of several changes you will see in the Division over the coming months.

Biological physics is one of the fastest growing and most vigorous areas of research in the APS. But because it has one foot firmly planted in biology while the other is strongly grounded in physics, the Division faces unique challenges. Among these is a diverse membership with varied tastes and requirements, a membership whose research often spans several APS divisions (DCP, DPOLY, DCMP and DMP come readily to mind). To this end the Division organizes a cross-divisional program for the March Meeting and works closely with the scientific community, in particular journals such as *Physical Review E* and the *Biophysical Journal*, to promote and to expand support for physics research in biology. You can help us in this effort by encouraging your colleagues and students to join DBP.

Several innovations are being introduced with this newsletter. The first is a series of articles profiling the work of some of the research groups whose members make up the Division. In each issue we will present these in-depth articles (two are included in this issue) and these articles will be archived on the DBP web site with links to the departments highlighted. In this fashion it is our hope to construct a living description of the research of the Division that may be used to recruit young people to both the featured research groups as well as to DBP.

Other articles will present the news and announcements of the Division. This month's news includes the minutes of the March Business Meeting as well as a synopsis of the Executive Committee Meeting. You will also find the Call for Symposia and Focus Sessions for the 2002 March Meeting.

The Biological Physicist will be published bi-monthly. Both Sonya and I welcome your comments. Letters to the editor may be published and ideas (or text) for articles may be submitted to her at bahar@neurodyn.umsl.edu. In the next months, we will be looking for research groups that want to highlight their work in a forum that is highly visible to their peers. If you are interested in writing such an article, please contact Sonya or me (mark.spano@mailaps.org).

Sincerely,

Mark L. Spano
Chair, Division of Biological Physics

Agenda Items from the Division of Biological Physics Executive Committee Meeting

Tuesday, March 13, 2001 at the Sheraton Seattle Hotel.

The meeting was opened at 7:45 p.m. The following Executive Committee members were in attendance: Ed Uzgiris, Mark Spano, Gene Stanley, Dan Gauthier, Paul Gailey, Bob Austin, Angel Garcia, Raymond Goldstein, Ken Dill, Bob Eisenberg, Sergey Bezrukov, Kurt Weisenfeld. Margaret Foster from *Physical Review E* and Judy Franz of APS also attended the meeting.

Agenda items included the following:

It was noted that Bob Callendar won the electronic vote for Associate Editor of *Biophysical Journal* representing DBP. A short discussion of the DBP role with respect to Biophysical Journal followed.

A report was given on the campaign to raise funds for the Biological Physics Prize.

It was reported that membership in the division is increasing. A membership invitation was distributed at the meeting to all attendees at DBP sessions. The effort resulted in 71 new members signing up at the meeting as of Tuesday.

It was reported that biophysics is the fastest growing area in FASEB and that DBP could provide a home for some of these researchers.

Margaret Foster was introduced and asked to report on biological physics reports in PRE. She passed out graphs showing journal statistics. The graphs showed that submissions are growing and the distribution of topics is broadening. She discussed electronic publication, which now occurs as soon as a manuscript is accepted and formatted for publication. It was pointed out that PRE will soon be splitting into two parts and that biological physics will mostly fill one part. It was requested that the division help recommend reviewers.

Overlap between PRE and the *Biophysical Journal* was discussed.

The proposed Division of Biological Physics Newsletter was discussed. It was asked that the minutes for this meeting be posted on the division web page along with the division bylaws. It was pointed out that specific names be removed from the minutes before posting.

A short discussion of the need for LCD (computer) projectors followed. It was pointed out that a significant fraction of speakers in DBP use the projectors, and that under the current procedures, rental of the projectors is quite expensive. No simple solution to the problem was found.

The meeting was adjourned at 10:00 p.m.

Minutes of the APS Division of Biological Physics Business Meeting

Wednesday, March 14, 2001, Seattle Convention Center.

Ed Uzgiris opened the meeting at 5:30 p.m. and reported on the Executive Committee meeting held the previous night. The three main points discussed were

(1) campaign to raise funds for the biological physics prize,
(2) efforts to increase membership (107 new members had registered so far this meeting), and
(3) the plans to provide a newsletter to the membership with information about meetings, funding opportunities, job openings, etc.

He then proceeded to present five certificates for new fellows of the division. The five new fellows were Rob de Ruyter van Steveninck, Dean Astumian, David Piston, Mark Spano, and Zaida Ann Luthey-Schulten.

He also encouraged nominations for next year and mentioned that the nomination window closes on April 1.

He then opened the floor for comments.

Comment #1: It was suggested that the division create a thesis prize if funds are available. It was pointed out that the prestige is more important than the money, and that some divisions offer an invited speaker slot to winners. Ed Uzgiris stated that the Exec Com would consider this idea.

Comment #2: A member asked if travel grants are available for graduate students. Mark Spano mentioned that no one applied for such a grant this year and that he would advertise this opportunity next year.

Ed Uzgiris pointed out that the division was interested in receiving more mini symposia proposals. A meeting attendee asked whether a schedule of symposia is available on the web. Mark Spano reported that he attempted to circulate a list of DBP sessions, but that APS was unable to send attached files to the membership. He added that he would post the schedule on the web in the coming year.

Comment #3: It was suggested that the division web site include a list of relevant granting agencies. Mark Spano replied that the division web site would include job listings and governance details including bylaws. He encouraged members to send their suggestions regarding content of the web site.

Ed Uzgiris announced the new Executive Committee members. The new vice chairperson is Ray Goldstein, the new APS council member (representing the DBP) is Bob Eisenberg, and new members at large are Angel Garcia and Ken Dill.

The editor of *Physics Today* requested suggestions for articles and pointed out that biological physics is a vibrant area. Margaret Foster from PRE reported that the journal is now indexed on Medline and reported on journal statistics.

Mark Spano (as incoming Chair) thanked Ed Uzgiris for his service. The meeting was adjourned at 6:00 p.m.

CALL FOR PROPOSALS FOR SYMPOSIA AND FOCUS SESSIONS FOR THE APS MARCH MEETING
MARCH 18-22, 2002
INDIANAPOLIS, IN
SEND TO ROBERT AUSTIN AT RHA@SUILING.PRINCETON.EDU
SYMPOSIA/FOCUS SESSION SUBMISSION FORMS WILL BE AVAILABLE ON THE DBP WEBSITE OR FROM PROF. AUSTIN.

The MIT Spectroscopy Laboratory by Dr. Irene Georgakoudi

Our work at the MIT Spectroscopy Laboratory (http://web.mit.edu/spectroscopy/www/), directed by Dr. Michael Feld, focuses on the development of novel spectroscopic techniques for the biophysical characterization of tissue. Such techniques have the potential to transform the field of medical diagnosis, offering powerful new means for quantitative tissue analysis, wide area surveillance, and biopsy guidance in a non-invasive way. Here, we describe in more detail a recently developed method for analyzing tissue spectra, called Tri-Modal Spectroscopy or TMS. TMS is the combination of three spectroscopic techniques, which characterize different aspects of tissue biochemistry, structure and morphology. Our aim is to use TMS to detect precancerous (dysplastic) changes, not easily detected with currently available technologies.

During standard endoscopic procedures, we acquire fluorescence spectra at eleven laser excitation wavelengths between 337 and 620 nm and one white light (350-750 nm) reflectance spectrum in less than one second. Light delivery and collection is mediated through an optical fiber probe. The acquired spectra contain information about the uppermost tissue layers, where almost 90% of cancers begin.

From the recorded fluorescence and reflectance spectra, we extract three types of spectroscopic information: intrinsic fluorescence, diffuse reflectance and light scattering. Intrinsic fluorescence spectroscopy (IFS) refers to the recovery of tissue fluorescence spectra that are free of distortions introduced by tissue scattering and absorption. To remove these distortions, we combine measured fluorescence and reflectance spectra using a photon-migration-based picture[1]. The extracted intrinsic fluorescence spectra are decomposed to provide quantitative information on the biochemical tissue composition and the changes that take place in pre-cancerous tissues (Fig. 1).

The measured reflectance spectra consist mainly of photons that are scattered many times before being detected. We use a model that is based on diffusion theory to describe the diffusely reflected light and, thus, to extract information about the absorption and the reduced scattering coefficients of tissue (diffuse reflectance spectroscopy or DRS[2]). The reduced scattering coefficient depends mainly on the morphology of the connective tissue, which provides structural support for the epithelium, the most superficial tissue layer. We observe consistent changes in the reduced scattering coefficient of dysplastic tissues (Fig. 2b).

A small fraction (2-5%) of the reflected photons are detected after undergoing single back-scattering events. The major target particles for this type of scattering are the nuclei of epithelial cells. Changes in the shape, size and number density of cell nuclei are histopathological hallmarks of dysplasia. Analysis of the singly-backscattered light spectrum using light scattering theory (light scattering spectroscopy or LSS), provides information about the size, and number density of cell nuclei (Fig. 2c) [3,4] without tissue removal or processing.

Since IFS, DRS and LSS provide complementary information about tissue biochemistry and morphology, their combined use, i.e. TMS, can serve as an excellent tool for

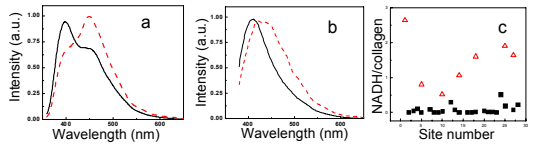

Fig. 1: (a) Measured tissue fluorescence spectra from non-dysplastic (solid line) and dysplastic (dashed line) Barrett's esophagus tissue sites. (b) Corresponding intrinsic fluorescence spectra. (c) Ratio of NADH to collagen fluorescence to the intrinsic fluorescence spectra of non-dysplastic (squares) and dysplastic (triangles) tissues.

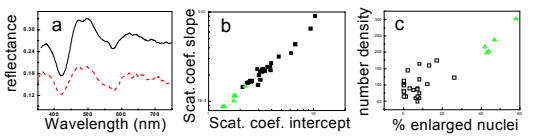

Fig. 2: (a) Measured reflectance spectra from non-dyspalstic (solid line) and dysplastic (dashed line) Barrett's esophagus tissue sites. (b) Slope and intercept of a line describing the wavelength dependence of the reduced scattering coefficient. (c) Nuclear number density plotted vs. nuclear enlargement. Non-dysplastic: squares; dysplastic: triangles.

biophysical tissue characterization and the detection of pre-cancerous lesions. Indeed, TMS is a superior tool for the detection of dysplastic changes in Barrett's esophagus [5] and the cervix.

Presently, we are testing software that is designed to perform TMS analysis in 4-8 s at the time of data collection. Thus, we can test directly the potential of this tool as a real-time guide to biopsy, and, ultimately, as a tool that could, in some cases, replace biopsies.

References

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The Real and Virtual Laboratory: A Conversation with Dr. Hans Braun

Early in the 1990s, student protest against animal use led the University of Marburg, Germany, to stop using experimental preparations in its practical physiology course. For course director Hans A. Braun, this led to a search for alternatives. How could the high standard of physiology instruction be maintained without experimentation?

Braun, who has been an APS Fellow since 1998 (cited for "the discovery of noise-mediated neuronal oscillators and for elucidating their nonlinear dynamical properties"), soon realized that a *virtual laboratory* was the answer. In collaboration with his then students Martin Hirsch and Martin Huber, Braun developed an interactive program called "MacFrog". The program was winning awards almost from its inception. In 1994 the software won the German/Austrian Software Award for the Best Teaching Software in Biology and Medicine, the Award for the Best Multimedia Application and also the MacWorld Editors Award for Trendsetting Multimedia Software.

Encouraged by this positive response, and by the support of Karlheinz Voigt, Director of the Institute of Physiology, Braun, Huber and Hirsch (who now runs a software company called interActiveSystems, www.brainmedia.de) expanded MacFrog into the first part of a software package called Virtual Physiology. Coverage of the program, "SimNerv", in the local media led to support from Apple Computers, and then from the Hessian State Ministry of Science and Arts (HMWK). Later, the group was awarded a grant from the German Ministry of Education and Science (BMBF), in combination with a grant from Thieme Publishers. This support allowed them to take SimNerv into its final form for public distribution, and to develop three more programs, SimMuscle, SimVessel and SimHeart.

The programs in the Virtual Physiology series, available in both English and German, reproduce exactly the experiments which had been done with real animal preparations in integrated physiology/pharmacology courses for medical students at Marburg. Today, the programs are in regular use in practical physiology courses in Marburg, used by nearly 300 students each semester.

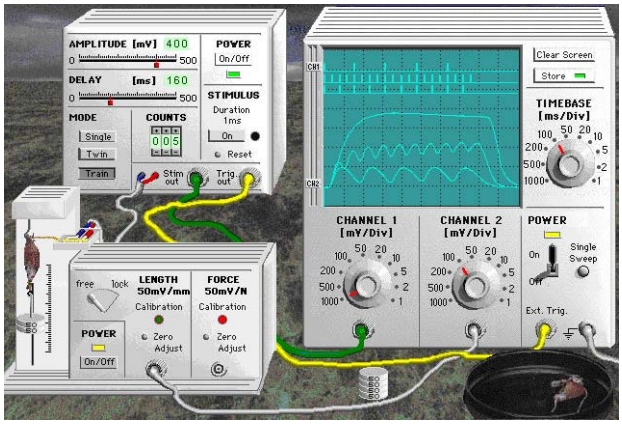
The programs offer an exquisitely detailed "in silico" laboratory for the student. In SimMuscle and SimNerve, video sequences demonstrate dissection of the frog and preparation of the isolated nerves and muscles, respectively. The student can then manipulate the experimental setup onscreen in order to "collect data" and reproduce classic experiments.

SimVessel combines physiological and pharmacological experiments which are done on isolated strips of the smooth muscle from vessels (aorta) and the stomach (antrum) of the rat. SimHeart presents an islotated preparation of the rat heart in the classical Langendorff set-up. The programs include a "chemistry lab" where students prepare the pharmacological substances

in appropriate dilutions for the experiments in the onscreen physiology/pharmacology lab.

A recently-added fifth program in the Virtual Physiology series, SimPatch, features all standard devices for doing patch-clamp experiments with mathematically simulated retinal cells. Patch clamp experiments were not included in the original practical courses, so SimPatch represents a teaching tool which allows students to experience aspects of the laboratory they would have been unable to participate in in a traditional course. Demo versions of Virtual Physiology can be requested from Theime Publishers at **www.thieme.de/elm/sim.** The software can also be ordered at a 10% developer's discount direct from Hans Braun (braun@mailer.uni-marburg.de).

More recently, in partnership with Voigt, Hirsch and H. Schneider, Braun is developing a new series of programs called "cLabs" ("computer laboratories"). This set of progams is still in a developmental stage, though demo versions should be downloadable from (**www.cLABs.de**) by the time this newsletter is posted on the DBP website. The idea behind cLabs, Braun explains, is to significantly expand on the Virtual Physiology series, including experiments which would be too difficult to be physically carried out within the context of a student's coursework, but are realizable in silico. For example, in the first virtual lab of the cLabs series, cLabs-SkinSenses, the



Like all the Virtual Physiology Software, SimMuscle offers a realistic laboratory setting for the student to explore.

student can record from different types of individual mechano- and thermosensitive skin afferent nerves. In the virtual lab the students will find an isolated piece of skin with 10 already preapared single fibre afferents. The student's task is to perform experiments to characterize the unknown receptor systems. Action potentials are shown on a virtual oscilloscope. The firing rate and interspike intervals are plotted on a virtual chart recorder along with the stimulus parameters. Virtual stimulation devices provide ramp-shaped or sinusoidal stimuli with preselectable amplitude and slope or frequency, respectively. Another program, cLabsNerv, provides a virtual laboratory for voltage and current clamp experiements, and also allows the students to design their own virtual neuronal networks. The latest versions of the cLabs software will be presented in the US at the next Society for Neuroscience meeting (San Diego, November 10-15, 2001).

Work on Virtual Physiology and cLabs has not slowed down Braun's research endeavors. Quite the contrary! The teaching programs also of the new cLabs series are closely related to current research at the Neurodynamics Lab. Analysis of sensory transduction in sensory receptors of the skin has been one of the major research themes in the Lab in recent years (see, for example, *Braun HA, Wissing H, Schäfer K, Hirsch MC, Oscillation and noise determine signal transduction in shark multimodal sensory cells. Nature 367: 270-273, 1994*). For other recent publications from the Lab, visit **www.uni-marburg.de/physiology/Braun/Neurodynamics.htm .**

The Laboratory's experimental and analytical research work has been supplemented for many years, especially due to the work of Martin Huber, with computer simulations of neuronal dynamics. The major focus has been on sensory transduction, but the models fit within a conceptual framework that includes modeling of higher systems dynamics such as psychiatric disorders. This latter project is a collaboration between current members of the Neurodynamics Laboratory and Martin Huber, who is now at the Department of Psychiatry and Psychotherapy at the University of Marburg, where he specializes in the study of the time-course of psychiatric disorders in collaboration with the Director of the Department, Jürgen Krieg. Their most recent work includes studies of the dynamics of recurrent affective disorders *(Huber MT, Braun HA and Krieg J, J Psychiatric Research 35:49-57, 2001).*

Braun's scientific work has had a very direct impact on the development of the teaching

software. For example, Skin Senses, apart from the virtual lab, additionally offers the possibility for doing interactive experiments using with recently published Hodgkin-Huxley-type cold and electroreceptor models (e.g., *Int J Bifurcation & Chaos 8: 881-889, 1998.*) which are presented in a form that allows the user to easily change control parameters such as dynamical noise, in order to explore their effects on the response characterisitics. The new programs include nonlinear-dynamics based analytical tools originally developed for research purposes, enabling the student to participate, not only in standard laboratory demonstrations and classic experiments, but also in some of the most recent applications of nonlinear dynamics to biological systems.

New Biological Physics Fellows Honored by APS

Five new Fellows of the American Physical Society (Division of Biological Physics) were inducted at the Division of Biological Physics Business Meeting.

- **Raymond Dean Astumian** of the University of Chicago, for his fundamental contributions to understanding the thermodynamics and mechanism of transduction of energy from a non-equilibrium chemical reaction to drive directed transport by molecular motors and pumps.
- **R. R. de Ruyter van Steveninck** of the NEC Research Institute, For contributions to understanding the physical principles of neural computation and coding through his elegant quantitative measurement and analysis of signals, noise and information flow in the fly visual system
- **Zaida Ann Luthey-Schulten** of the University of Illinois, for her contributions to the field of protein folding including elucidating its basic mechanism and developing optimized energy functions for protein structure prediction.
- **David William Piston** of Vanderbilt University, for outstanding contributions to the development, application, and dissemination of quantitative spectroscopic methods to the imaging of proteins and small molecules, their environment and their interactions within single living cells.
- **Mark L. Spano** of the Naval Surface Warfare Center, for his achievements in experimental nonlinear dynamics, especially as applied to biological systems such as the heart and the brain.

→ *New APS Fellows congratulated by outgoing DBP Chair Ed Uzgiris (far right). New fellows, from left to right: Mark Spano, Dean Astumian, R. R. de Ruyter Van Steveninck and David Piston. Also honored was Zaida Ann Luthey-Schulten, who was not able to attend the ceremony.*