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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?

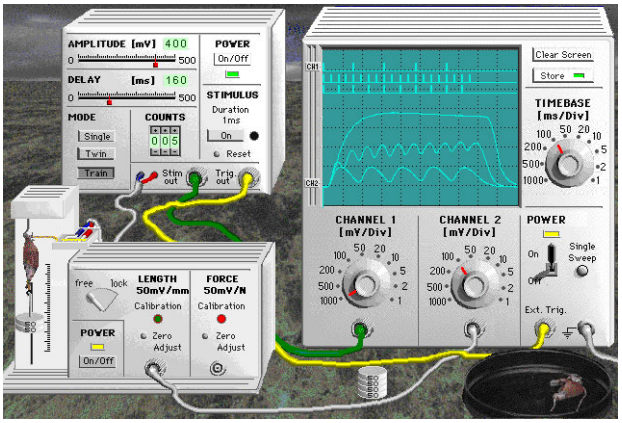
Braun, who has been an APS Fellow since 1998 (cited for "the discovery of noise-mediated neuronal oscillators and for elucidating their nonlinear dynamical properties"), soon realized that a *virtual laboratory* was the answer. In collaboration with his then students Martin Hirsch and Martin Huber, Braun 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.



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

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, see also **www.cLABs.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 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

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.