NEUROPHYSICS

Logic gates come to life

Nerve cells have the ability to self-organize into strongly interacting networks, even when grown in a Petri dish. Controlling the geometry of such cell cultures might be all that is needed to set up neuronal computing devices.

Fred Wolf and Theo Geisel

are at the Max Planck Institute for Dynamics and Self-Organization, the Bernstein Center for Computational Neuroscience and the Faculty of Physics, University of Göttingen, Bunsenstrasse 10, 37073 Göttingen, Germany.

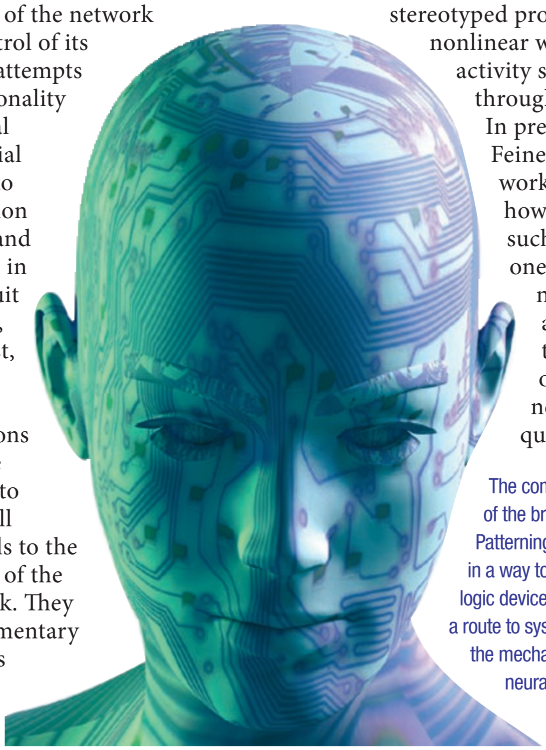
e-mail: geisel@nld.ds.mpg.de; fred-wl@nld.ds.mpg.de

As you are reading these lines, millions of neurons in your brain are activated. In some still rather opaque way the collective dynamics of these millions of neurons effectively computes subject, predicate, object, and so on, from the stream of observed letters for each sentence, allowing you to understand what is written. It is one of the major aims of neurophysics and theoretical neuroscience to understand the laws governing the collective dynamics of large biological neural networks and to determine how they carry out complex computations. For developing a physics of biological neural network computation it is desirable to have laboratory experiments in which neuronal circuits perform a prescribed computation under physically and chemically well controlled and reproducible conditions, such that the biophysical, cellular and network mechanisms underlying their performance can be dissected experimentally. Ofer Feinerman and colleagues have made a step in exactly that direction: on page 967 of this issue they report[1] a surprisingly simple experimental approach to reproducibly growing neuronal cell cultures that can be designed to perform any desired computation.

Living networks of neurons grown in cell culture represent a promising path towards an experimental neurophysics of neural computation — cultured networks of mammalian neurons are grown routinely in hundreds of laboratories around the world, and over the past ten years it has become possible to monitor their activity patterns with sufficient precision to obtain a quantitative phenomenology of their collective activity states[2–4]. Recent data indicate that it is possible to 'train' such networks to react selectively to external stimulation[5], and some groups have even started to build hybrid closed-loop systems of cultured networks and robotic components, in which the network operates as a kind of biological robot brain[6]. Despite these efforts, no approach has yet been found for setting up a computing device from living neurons in a standardized and reproducible manner, let alone for rationally designing such devices for a prescribed purpose.

This gap is now filled by the work of Feinerman *et al.*[1]. The key to their success seems to be the correct balance between self-organization of the network and external control of its layout. Previous attempts to achieve functionality in cultured neural networks by spatial patterning tried to impose the position of every neuron and every connection in the growing circuit (see, for example, ref. 7). In contrast, Feinerman *et al.* only impose the geometry of regions in the dish where neurons are able to grow, and leave all connection details to the self-organization of the emerging network. They present three elementary geometric layouts that cause the developing network to operate reliably as either a threshold element, an AND gate, or a neuronal diode. Because these components can be composed into a so-called NAND gate, this set of basic elements is in principle sufficient to set up any desired logical circuit. By daisy-chaining 50 of their neuronal diodes, Feinerman *et al.* also designed a neural oscillator that can be used as a clock or memory device. Their systems thus contain all elements needed to assemble a Turing-universal computer.

The fact that the operations performed by these devices are predictable and reproducible is a result of their reduced dimensionality. Networks grown as extended two-dimensional carpets can show complicated activity patterns that are often hard to predict[3,4]. When restricted to growth in narrow stripes, however, the network connectivity becomes effectively one-dimensional and the dominant form of activity is stereotyped propagating nonlinear waves of electrical activity sweeping through the culture. In previous work, Feinerman and co-workers[8] established how to generate such effectively one-dimensional neural networks and analysed the dynamics of the emerging neuronal waves quantitatively. To the delight of theoreticians they found that the dynamics of these waves agreed very well with the quantitative predictions of relatively simple mathematical network



The computational capability of the brain remains a mystery. Patterning living neurons in a way to form functional logic devices might provide a route to systematic study of the mechanisms underlying neural computation. © iStockphoto/Antonis Papantoniou.

models[9]. Once collective neuronal activity occurs in the form of propagating nonlinear waves with reproducible properties, it becomes possible to design schemes for their propagation and collision that realize logical operations such as the three elementary devices of Feinerman and colleagues[1].

So, is your next iPod likely to run on neuronal cell cultures? With elements in the millimetre range, cycle times on the order of a second and a substantial probability of failure after some dozens of successive operations, it appears that 'neuro-logic' devices will not be in a position to outperform conventional computing systems any time soon. But that is not the issue. Neuronal logic devices will enable a new type of neurophysical experimentation that was inconceivable before and is promising to provide fresh insight into several unresolved issues in neuronal computation. One of these is how neuronal circuits can operate reliably while their basic constituents, the synapses, are stochastic elements. The work of Feinerman *et al.*[1] already goes some distance towards answering this question by building a quantitative model that reproduces the behaviour of all elementary devices, quantitatively explains their measured error rates, and reveals how redundancy and multiplexing lead to reliable mesoscale behaviour even if each synapse fails to transmit a signal every second time. This groundwork should enable future studies to probe the transition from unreliable microscopic to reliable mesoscopic behaviour in neuronal systems in more depth than has previously been possible. Nevertheless, it is legitimate to wonder whether studying such *in vitro* neural circuits is likely to teach us anything about computation in real brains. The answer to this question might well be more affirmative than the distinctly technomorphic non-organic appearance of the cultures may at first suggest. A long-standing controversy in theoretical neuroscience concerns the question of whether waves of neuronal spike activity propagating through complex but essentially one-dimensional networks called 'synfire chains' exist or even have an important function in neural computation[10–12]. The computational capabilities and limitations of such systems have in the past attracted substantial attention in theoretical studies. As assembled neuronal logic devices are 'synfire computers' in effect, the capabilities and limitations of synfire-type neuronal information processing can now be examined experimentally with real biological neurons. The systems presented in the new study represent a solid stepping stone for approaching such key questions in neural computation in well-controlled quantitative neurophysics experiments.

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BOSE–EINSTEIN CONDENSATES

A peek and a poke

An adapted scanning electron microscope allows the non-destructive measurement and manipulation of Bose–Einstein condensates. The single-atom sensitivity that this technique promises could soon become indispensable in the study of quantum degenerate atomic gases.

Dieter Jaksch
is in the Department of Physics, University of Oxford, Clarendon Laboratory, Parks Road, Oxford OX1 3PU, UK, and at the Centre for Quantum Technologies, 117543, Singapore.
e-mail: dieter.jaksch@physics.ox.ac.uk

Light is the main tool currently used to measure the properties of Bose–Einstein condensates (BECs) and other ultracold atomic gases. Because the wavelength of even soft X-rays is not much smaller than the size of the atom cloud, there are strict limits on what can be done with light. On page 949 of this issue, Gericke and colleagues demonstrate a radically different approach[1] — instead of light they use the beam of a scanning electron microscope (SEM) to probe and manipulate a BEC. In principle, the technique allows an improvement of several orders of magnitude in the resolution with which BECs and related systems can be imaged. Moreover, by doing so in a way that is less destructive than most conventional optical approaches, it could lead to significant new insights into the physics of quantum degenerate ultracold atomic gases.

The spatial resolution of conventional optical microscopic techniques is limited by diffraction to half an optical wavelength — typically of the order of a few hundred nanometres. Some improvement beyond this value can be achieved by operating at ultraviolet and even X-ray wavelengths, through near-field imaging approaches and even by clever exploitation of the emissive behaviour of single-molecule fluorescent dyes[2]. However, such approaches tend to be applicable to only certain systems, and even reaching spatial resolutions below a few micrometres can be technically challenging.

Certainly, the development of the use of light for studying ultracold quantum degenerate gases, such as BECs, is already close to its practical limits. The total size of these systems is determined by the trap in which they are confined (be it a conventional magneto-optical trap or that of a so-called atom chip), which is typically just a few micrometres across. To ease the situation and enable some information to be gained about the structure of the gas in such a trap, a