

Look at biological systems through an engineer's eyes

SIR — Your Connections series of Essays has taken some interesting looks at the interdisciplinary study of complex, dynamic systems (see www.nature.com/nature/focus/arts/essays/index.html). However, it has not featured a discussion of the physiological tradition of biological research, in which biological systems are analysed using reduced descriptions in much the same sense that an engineer uses a reduced description of an amplifier. An engineer is often not interested (to first order) in what is inside the box that produces gain, but studies the properties of the gain, its linearity, its frequency dependence and so on. A complete description of the structure of the amplifier is far less useful than a reduced description of its input–output relation, when the goal is to use the amplifier or connect it to other devices to make a system.

An engineer told that an unknown black box is an amplifier is rather like a biologist confronting an unknown biological system. Some structural knowledge is indispensable. Engineers would have a terrible time if they did not know which leads were power supplies, which inputs and which outputs. But the last thing an engineer would want to know is the complete circuit diagram, let alone the locations of all molecules or atoms in its resistors, capacitors and transistors. Successful investigation requires some (indispensable) knowledge of structure; but it requires many more measurements of inputs and outputs, under many conditions. Successful investigation also requires a good quantitative model of the system, called a device equation.

Physiologists have successfully analysed a large range of biological systems using this 'device-oriented' approach. For more than a century, medical students have used it to learn that the kidneys filter blood to make urine; the lungs transport oxygen from air to blood; muscles contract; sodium channels produce action potentials; and so on. Each device description in physiology — on each length scale from organ, to tissue, to cell, to organelle, to protein molecule — is associated with a device equation, just as a device description in engineering (for example, of a solenoid) is followed by an approximate device equation for its function, for example, its input–output relation.

No one knows which biological systems can be viewed productively as devices. No one knows how many of the unsolved complexities of biological research reflect problems of the reverse engineering of simple devices, and how many reflect the inherent complexity of biological systems. One can certainly imagine simple systems that are hard to investigate because of the paucity of

experimental knowledge. Complex systems — for example, with many internal nonlinear connections like the integrated circuit modules of digital computers or, perhaps, the central nervous system — may not be easily analysed as devices, no matter how many experimental data are available. But it seems clear, at least to a physiologist, that productive research is catalysed by assuming that most biological systems are devices. Thinking today of your biological preparation as a device tells you what experiments to do tomorrow.

Asking the questions in this way leads to the design of useful experiments that may eventually lead to the device description or equation, if it exists. If no device description emerges after extensive investigation of a biological system, one can look for other, more subtle descriptions of nature's machines.

R. S. Eisenberg

Department of Molecular Biophysics and Physiology, Rush Medical Center, 1653 West Congress Parkway, Chicago, Illinois 60612, USA