have signaling domains that are serine-threonine kinases, phosphoprotein phosphatases, or guanylyl cyclases. In several instances, intermolecular interactions between signaling cassettes are critical to activation: Homodimer formation is clearly essential for the activity of the protein kinase that is regulated by Tar (7), and phosphorylation of one subunit of the insulin receptor by the other is critical for signaling (5).

There seems to be little specificity between sensing and catalytic domains; almost any combination works. Nature herself has produced a huge variety of pairs of signaling and sensing domains, and researchers have added to the collection with the construction of artificial (and functional) chimeras. The sensing domain of Tar fused to the signaling domain of the human insulin receptor yields a chimeric receptor with tyrosine kinase activity regulated by aspartate (8). This versatility has supported the notion that type I receptors make use of a simple and extremely robust mechanism for transmembrane signaling. Stimulatory ligands are thought to regulate intersubunit interactions between sensing domains at the outside surface of the membrane to control intersubunit interactions between signaling domains on the other side of the membrane. The simplest case would be a ligand-induced monomer-dimer transition. But, at least for some receptors, this mechanism is clearly an oversimplification; insulin receptors or Tar proteins with intersubunit disulfide cross-links between sensing domains can still be regulated by stimulatory ligands. In these cases, it has been posited that the relative orientation of monomers within a preexisting dimeric structure is responsible for signaling (1, 9).

In molecular biology, the ultimate test for any hypothesis is genetic. The two reports in this issue describe genetic studies of Tar function which demonstrate that heterodimers with one signaling domain deleted can still function normally (2). The authors asked the question, "What is the sound of one hand clapping?" by genetically deleting one hand. Amazingly, the result of this Zen-like experiment was not an imponderable silence but loud applause—a robust cellular signal. These findings call for reexamination of the basic assumption that Tar functions as a dimer. In fact, although there is ample evidence that the ligand binding domains can exist as dimers, the isolated signaling domain of Tar appears to be a loosely folded monomer. It is only when Tar monomers associate into a complex with the histidine kinase that the signaling domain assumes its functional form. Moreover, it has been shown that in cells, Tar is localized with the protein kinase and other auxiliary signal-transduction proteins in a complex or a patch that contains hundreds of receptor monomers (10).

What are the implications of these results with Tar for other type I receptors? One might argue that Tar is different, and that these results are not generalizable. And it is true that Tar is unique: It has an NH_2-terminal transmembrane extension that is absent in most type I receptors; it is specifically designed to solve a unique problem; and it is bacterial. But every type I receptor has its own unique structural, functional, and phylogenetic features. Nevertheless, all share with one another and with Tar the same set of mechanistic properties common to transmembrane signaling. Moreover, we need not look far for natural type I mammalian receptors that function as heterodimers with one subunit lacking a signaling domain just like the engineered variants of Tar described in this issue. Well-known examples include the nerve growth factor receptor, as well as several interleukin receptors that are closely related to hGHR (5).

A receptor signaling complex is a dynamic two-dimensional array of sensory elements that project through connecting transmembrane helices onto a network of signal-transduction components at the opposite side of the membrane. The portions of the receptors in the cytoplasm are ill-defined compared to the ligand binding domains at the surface, but it is known that they participate in complex interactions with a variety of signal-transduction components. Besides being regulated by ligand binding domains from without, receptor signaling networks are also controlled by intracellular feedback and feedforward mechanisms from within. This property gives these systems a plasticity that may in part account for the functions of dramatically altered receptor variants. Perhaps, in light of these considerations, our view of type I receptors as couples waltzing freely in a lipid sea should be supplanted by a new paradigm in which the music and the motions involve a much more complex choreography.

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The World Wide Web as an Instructional Tool

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The Internet was born in December of 1969 (1) and has grown phenomenally since (2–4). Its graphically attractive, user-friendly modality, the World Wide Web (WWW), is younger and growing even more explosively (5–7). By its nature, the WWW is a tool ideally and uniquely suited for the advancement of education.

The WWW is composed of multiple computer "servers," which can send documents or "pages" to Internet users who navigate from server to server by means of Web-browser software. Web documents can contain text, sound, pictures, or movies, and they can be interactive. Traditional paper-bound tasks—searching large databases or completing questionnaires—can be replaced by WWW-based technology. Harnessing the multimedia and interactive features of the WWW in conjunction with its vast store of information is presently the premier challenge to educators.

There are three ways in which the WWW can be used for educational purposes (8). The first relies on the student's (or client's, in WWW terms) ability to access information. This information can be general—for example, the prodigious quantities of information organized at indexing sites such as Alta Vista (6) and Yahoo (7)—or specific—such as the large quantities of specialized informa-

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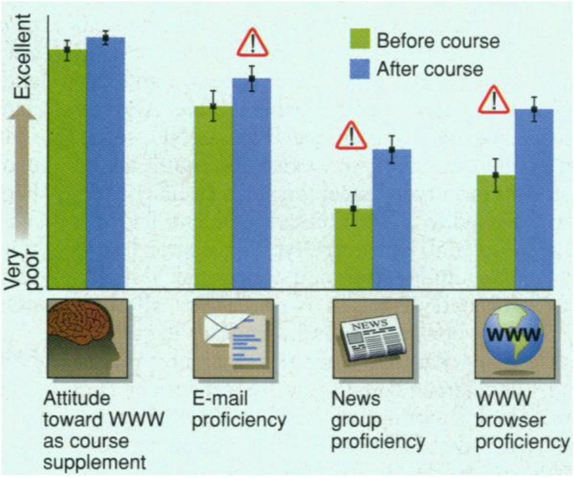
tion on neuroscience (9). As an example of the latter, a comprehensive overview of the neurosciences is cataloged on the Internet at the "Neurosciences on the Internet" WWW site (10). This site accesses various university libraries and neuroscience discussion groups and even allows the dissection of a virtual frog (11). In this case the WWW becomes a 15 billion–word encyclopedia.

Along with this access comes the inherent drawback that there is no reliable editor to raise the signal-to-noise ratio of the information, so portions of the WWW are much more useful than others. One possible solution to the cacophony of noise on the Internet has its origins within the research and educational communities. Academic journals are slowly being supplemented and supplanted by the electronic journal, often a searchable, interactive, multimedia WWW version of the paper journal. Motivated by exorbitant journal prices, long publishing delays, and a promising new medium, innovators have pioneered a movement that now realizes nearly 1000 electronic journals on the Internet (12). Proliferation of the electronic journal has now passed the critical point where its permanence is no longer a question, but many issues remain unresolved: the mechanics of peer review, financial support of electronic media, copyright, database sharing, and reluctance to submit to cyberspace. Until these questions are resolved, the virtual journal will remain in evolutionary flux.

The second way in which the WWW can be used in education is as an integrated interface for distance learning, often called the virtual classroom. Here an instructor at one location electronically educates students from anywhere in the world. Groups such as the Open University, University On-Line, or CALCampus (13) are transforming regular university classes into a digital format, where lectures are video recorded and replayed either live or delayed through a Web browser. These digital lectures can be complemented with graphics, digitized images, computer simulations in real time, and other sorts of educational aids not normally found in the nonvirtual lecture hall. Removing the social aspect of the physical classroom and requiring students to motivate themselves to attend virtual lectures has obvious drawbacks, but the major hindrance to this practice is the current state of Internet technology. The technical limitations on the speed and quantity of information delivered to a Web client is too slow as yet to make the virtual classroom a viable alternative to the real classroom.

The third way in which the WWW can be used is to supplement the conventional classroom rather than replace it. By combining the immense quantity and spectrum of information within the WWW, the interactive capabilities of a Web client, and the multimodal nature of Web pages, the WWW can be an instructional aid for a conventional class. Each segment of a lecture course can be given an Internet component. The academic concepts are extended and reinforced, and as an added benefit, supplemental Internet skills are imparted to an Internet-naïve student population (see figure). For example, a WWW site acted as an adjunct to a 123-student, upper division neurobiology course at the University of California at Berkeley (14). This site includes searchable lecture outlines, a discussion group, links to WWW sites associated with class material, class surveys, regular e-mail announcements, examination answers, interactive grade retrieval, searchable term papers, and course assignments involving the WWW. One assignment required that each student electronically submit a term paper for anonymous peer review. Every paper was placed on the Internet anonymously and was randomly reviewed by two other students, also unnamed. This task required 2460 pages of text to be read and reviewed over the Internet, all done automatically (98.4% of the students completed the assignment). At the end of the semester, 88% of the students stated in course reviews that using the WWW significantly aided their understanding of the concepts presented in class, and 88% also reported that their knowledge of the Internet and its functioning (that is, their use of e-mail, news groups, and Web browsers) increased (see figure).



Extending the lecture hall. The results (± SEM) of a survey administered to an upper division lecture class at the beginning (green bars) and end (blue bars) of the Spring 1996 semester at the University of California at Berkeley. !, $P < 0.05$.

An enhanced version of this Perspective, with live links, can be seen in *Science* Online on the WWW at http://www.sciencemag.org/

The potential for the WWW to contribute in each of these three ways is enormous. But until certain technological requirements are met (for example, the ability to instantly access complex graphics and videos), the WWW will best serve as a course supplement rather than a classroom replacement. For the future we will need to address questions such as how issues surrounding intellectual property and academic honesty are to be resolved. Besides a presumption of integrity, what prevents students from another university from presenting as their own work any term paper found on the Internet? What will instructors do to prevent plagiarism? What guarantees will a student have that their personal information or intellectual property will not be scattered through the electronic universe? With the Internet anticipated to expand 1000% over the next few years, we must find answers to these procedural and ethical questions.

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