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THE FIRST WOR

BIG FISH AND LITTLE FISH

few years back, Sen. Albert Gore (D-TN) was talking about legislators' propensity for legislating. "When the only tool you have is a hammer," he said, "every problem begins to look like a nail."

That reminds us of a classic test of problem-solving ability: The subject is put into a room with a 30-foot ceiling. From the ceiling hang two lengths of string, each 30 feet long. The strings hang 36 feet apart. Otherwise the room is completely bare. The subject is given a hammer, and told to use it to fasten the lower ends of the string together.

The "correct" solution, of course, is to tie the hammer to one of the strings so that it just clears the floor, displace the new-made pendulum bob to the midpoint between the two strings, give it a little push, scurry over to the other string, grab it, and scurry back in time to catch the hammer on its return (while trying not to let it hit you in the eye).

The problem, you see, is that a hammer is not always a hammer. Much less

is every problem always a nail.

And that, in part, is why this month's issue carries two articles on the nonprotein aspects of drug design: We may be too used to looking at a bioactive protein and thinking that this molecule, or a minor modification of it, is the product we have been looking for.

This came up the other day while we were talking to a friend in the separation business, trying to think about where the biotechnology-based industries are going. A disturbing question popped up: Will developing non-protein biotechnologies put a natural cap on the market for any

protein therapeutic?

Consider: According to Ron Nordmann, a PaineWebber pharmaceutical industry analyst, 10 of the world's 10 best-selling pharmaceuticals are oral formulations. Thus, as the potential of an injectable protein increases, so does the incentive for developing an orally stable, cheaper-to-produce nonprotein analog—a drug that (if effective) would likely take over the protein's market and create a much wider demand as well.

Yet the market for protein-based therapeutics will surely expand. The flexibility of the production systems and the wide variety of effects possible from proteins will guarantee their expanding use in treating conditions that will be better and better understood, and more and more narrowly defined. In a sense, the pharmaceutical market could become a rookery of small niches. And proteins, with what we expect will become direct discovery and development pathways, will occupy about one niche in ten.

But for some of the really big products, the grim thermodynamics of money may drive the process towards sophisticated organic synthesis. Research costs and process development will probably grow, but production costs will probably drop, productivity may rise, and the market expand greatly.

The big pharmaceutical companies are placing heavy bets on a roundabout, biotechnology-driven return to organic synthesis for their big products three or four generations down the line. It is equally clear that those developments will not be possible without the detailed knowledge of biological activity being developed at the small companies.

New Frontiers

We note with glee that one of these two forward-looking articles is written by John N. Hodgson, Bio/Technology's new London-based senior editor. John (formerly editor of the review journal Trends in Biotechnology) is our first full-time writer based outside the U.S., and he joins Bernard Dixon to give this publication the finest biotechnology team in Europe.

Mr. Hodgson's Bio/Technology assignment coincides with the appointment of our first European Publisher, improbably and unrelatedly also named Hodgson (Helen). These initiatives mark what is for us an important milestone in balancing our coverage of this worldwide pursuit, yet the territory is also familiar: Our parent company is London's Macmillan Magazines, so we are in effect opening up a new frontier on the old --- Douglas McCormick homestead.