by Bernard Dixon

SPIDERWEBS, FLEAS' LEAPS, AND SILKS

Louis Pasteur's formidable esteem among most of his scientific peers is epitomized by a request he received in 1865 from Jean Baptiste Dumas. Would the 43-year-old French chemist, fresh from researches into lactic and other fermentations, please investigate the disease that was devestating silkworms and thus an entire industry in the south of their country? Pasteur had never seen a silkworm in his life—nor even a mulberry tree, source of the leaves on which the insects feed. Yet he accepted the challenge, justified Dumas's confidence, and thereby convinced himself that epidemics could be conquered by applying rational principles.

Not only that. As René Dubos observes in his splendid book *Louis Pasteur-Freelance of Science*, more than acute perspicacity and dogged effort were required. "To make his work of value to the silkworm breeders, Pasteur had to display the qualities of a successful industrialist concerned with economic necessities as well as with practical problems; he had to be always ready to meet objections, always willing to adapt his language and procedures to the limited intellectual or scientific equipment of his public." As with the medical breakthroughs for which he later became more widely famed, Pasteur approached his biotechnological task in the Alais district of France very much in the spirit of someone pursuing applied science today.

I don't know whether Trevor Jarman, Technical Manager in the Biotechnology Group of PA Technology, has reflected upon the unlikely scenario of the discoverer of molecular asymmetry being invited to study pebrine disease in *Bombyx mori*. But there was a similar element of unexpectedness in this young Britisher's decision to focus attention on the same insect during Biotech 85, held recently in Geneva. Jarman did so because *Bombyx mori* generates a type of fiber which he believes is of high importance to biotechnologists.

Despite its partial replacement by nylon after World War II, and by other synthetics since then, silk remains an extraordinarily valuable material. It is strong, resisting breaking by weights up to four grams per denier; can be stretched by 20 percent before snapping; is more heat resistant than wool; and has other excellent moisture absorption and dyeing properties. Jarman's suggestion is that silk—or rather silks, because they occur in rich profusion—could now be manufactured more efficiently and profitably by genetically engineered micoorganisms. Along with other animal and plant proteins such as collagen, elastin, resilin (which stores mechanical energy in insects' wings and fleas' legs) and abductin (from the hinge ligament of bivalves), silks are candidates for commercial production based on the transfer of the appropriate genes into bacteria. Many such natural proteins could be modified for a wide range of different uses, Jarman believes. Yet they have been virtually ignored so far as potential products of biotechnology.

The silk fibers generated by Pasteur's *Bombyx mori* are composed of twisted strands of fibroin, coated and held together by another protein (sericin) which is removed during conventional manufacturing. The primary component of fibroin's complex structure is a huge polypeptide with tandem arrays of highly crystalline regions interspersed and flanked by a matrix of more amorphous regions. The amino acid sequence in the crystalline parts is simple, consisting mainly of alanine and serine alternating with glycine. The amorphous parts contain residues with bulky side chains which destabilize the regular structures. Although silk's physical properties are influenced by the manufacturing process, they also correlate with amino acid composition and distribution—as far as these are known.

Trevor Jarman's enthusiasm for microbial production of such biomaterials is based partly on knowledge of this sort, which raises posibilities for subtle modification. But it also stems from an awareness, common among zoologists but not biotechnologists, of the immense range of structural proteins already to be found in nature. He points, for example, to the variety of silks made by other arthropods. "Some spiders use up to five different silks for their webs and cocoons," Jarman observes. "Each is adapted to a particular function, whether as a dragline, like a climber's safety rope, or as a sticky spiral web to ensnare the spider's prey. These contrasting roles for silks require corresponding physical properties in terms of strength, extensibility, and visco-elasticity. In turn these differences reflect, at least in part, variations in amino acid composition and distribution."

There was some skepticism, among the Biotech 85 audience, as to whether the large-scale microbial manufacture of biopolymers like silk could ever be commercially viable. Jarman insists that the likely costs are not out of line with those for more specialized gene products being evolved today in far smaller quantities. Depending upon the efficiency of production and recovery, he estimates the cost of one ton of biopolymer at about $1000–5000. Allowing for the necessarily high investment in development work and equipment, written off over a period of ten years, he puts total manufacturing costs at about $10,000 per ton for an annual ouput of 1,000 tons and up to $10 million dollars per ton on a 100 kilogram per annum scale.

Those are daunting figures. But they are not *too* daunting, especially if we bear in mind future uncertainties over the price of petroleum, on which existing fibers are based. And what Trevor Jarman's listeners in Geneva did not contest was the principle of surveying the natural world for modern equivalents of the wood, leather, cotton, and wool with which man has clothed and housed himself in the past. Particularly as we develop greater insight into the relationships between molecular structure and physical performance, the possibilities are surely immense.

Bernard Dixon, Ph.D., is a contributing editor of *Bio/Technology*.