Electronics and Biotechnology

How new advances in technology will lead to innovative sensors and more

Christopher MacLeod

We are living in the midst of a quiet revolution. It's a revolution that's every bit as important and profound as the one in Microelectronics which preceded it. However, because it hasn't started to effect our daily lives yet, most of us are scarcely aware of it. It's a revolution in Biotechnology.

In the last few decades, scientists have discovered how to manipulate and fingerprint DNA - the very core of life itself. It can now be changed and reintroduced into other organisms, effectively creating new species of plants and animals. We have even mapped the human genome and cloned animals from adult cells - until recently the stuff of Science Fiction. Development is proceeding at a breathtaking pace.

This technology, more than any other, will change our lives in the 21st century - mimicking the growth of electronics in the 20th. However, that change will only be complete when Biotechnology unites with our other great technological achievements - Computing and Integrated Circuit Electronics. This article is about one way that might happen.

Wetware

At the moment Biotechnology is still *wet* - it's done by skilled technicians in chemistry-lab test-tubes. The next stage of its development is to integrate it with the power of microelectronics and computing and move it out of the lab and into industry, the doctor's surgery and even the home - for it to become Bioelectronics.

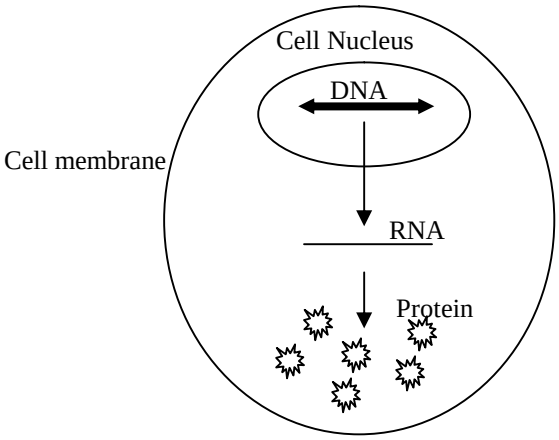
However, there is a practical problem. Up until now, biochemists and engineers have been living in their own separate worlds and their paths have seldom crossed. This means that there is a lack of communication and understanding between them. They effectively speak different technical languages and use different concepts - very few people are trained in both disciplines. To understand how integration can take place we first have to understand the technology and what it can do for us - and this means we have to look at a little chemistry.

First, some biochemistry

Our bodies, like those of all other organisms, are made from cells. Each cell is a living chemical factory. It takes raw materials from the outside world (mainly carbon dioxide, light and water in the case of plants and various foods in the case of animals) and manufactures complex products from them - cotton, wood and skin are examples.

Each cell works in basically the same way. It has a built-in code - the DNA. This code is continually being read by another chemical, called RNA; this, in turn, goes to make the chemical workhorses of the cell - the proteins. Figure 1 illustrates the process.

Figure 1. How the DNA code of the cell makes proteins.

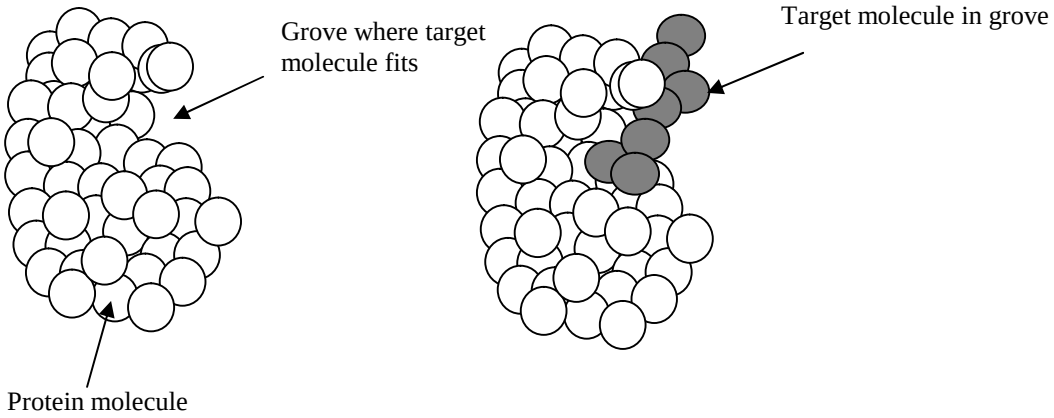


It's the proteins which are the most important part of the system. They do all the work in the cell - making new material, breaking up old, and sensing and signalling changes in the cell's environment.

Proteins are the key

All useful proteins bind to other chemicals. Some synthesise new molecules by joining their component parts together; others break up them up - such proteins are called Enzymes. They manipulate chemicals at the atomic level - how they work is illustrated in figure 2. The atoms which make up the protein have a particular physical shape which is so precise that only the correct target chemical can fit into it.

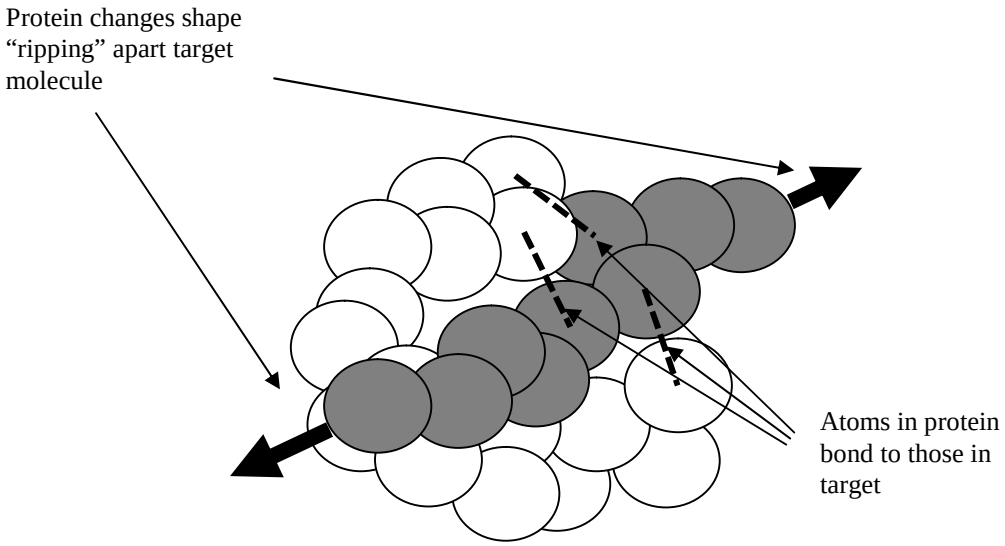
Figure 2. Proteins bind to other chemicals because they have the correct shape.



Often the shape is a type of "grove" in the atomic structure of the protein. Enzymes which synthesise new chemicals work by letting the simpler molecules attach to the protein in such close proximity that they bond together to form a polymer. This process allows the synthesis of highly complex and useful chemicals which could not be made any other way because of the high energy and difficulty involved in forming the bonds.

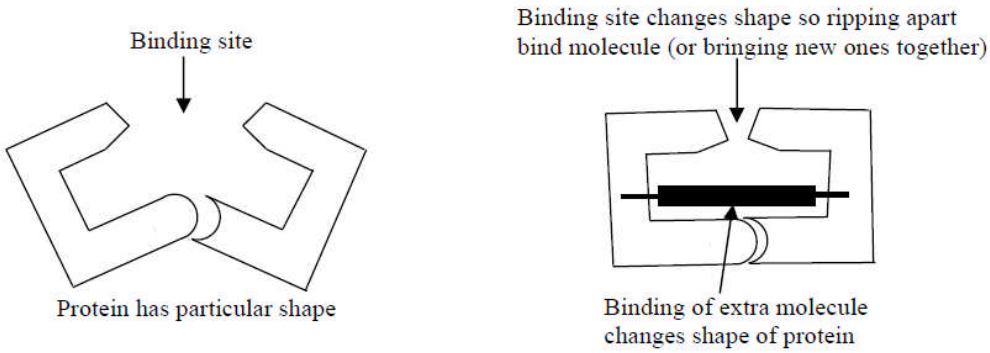
Those which break down chemicals do the opposite, allowing a molecule to bond and then breaking it apart as shown in figure 3.

Figure 3. Protein bonds rip target molecule apart.



Both this and synthesis are often helped by the thermodynamic movement of the protein or by a third chemical attaching elsewhere on the protein - which changes its shape, so ripping apart the bound molecule. Commonly this third chemical is a substance which contains a "high energy" bond - one which has the capacity to release a large amount of energy when broken. The most common substance with this ability is called ATP (Adenosine Triphosphate). Figure 4 shows the idea.

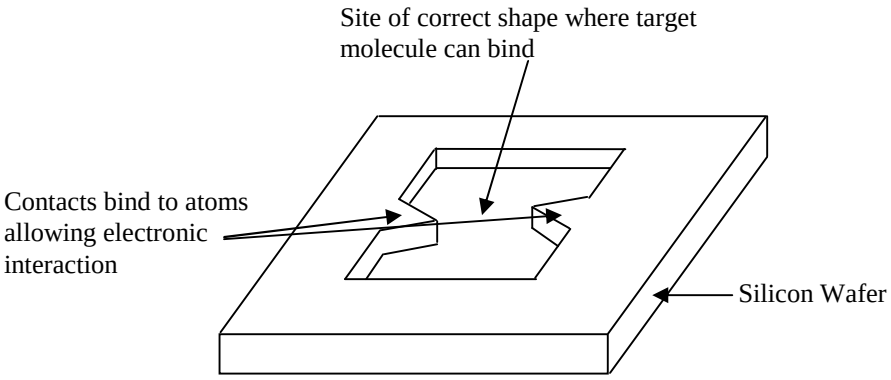
Figure 4. Attachment of another molecule changes the protein's shape.



Making electronic proteins

Since proteins are the key to biological systems, all sorts of possibilities open up if we can work out how make controllable artificial ones. The logical way to try and do this electronically is on a silicon wafer. In theory we could make binding sites on a chip as shown in figure 5. The trouble is that the atoms which make up the binding groves of real proteins are far too close together to be fabricated using standard photolithography. Atom diameters are measured in angstroms (10^{-10}m); whereas we can only routinely fabricate features of tens or hundreds of nanometers (10^{-9}m).

Figure 5. An electronic protein.

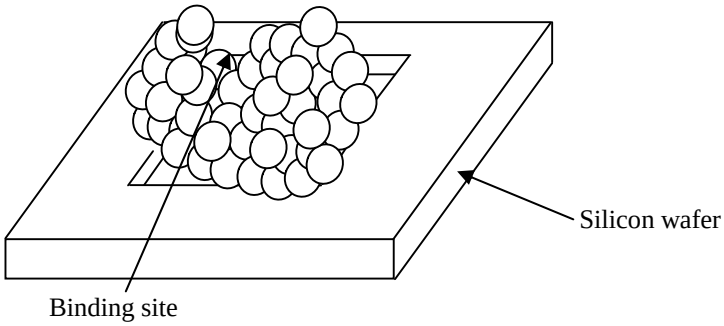


However, there is hope - and it's coming through research in the new science of nanotechnology. Already scientists have used Atomic Force Microscopes to manipulate and reorder the individual atoms of a silicon wafer - even writing words with single gold atoms. Such technology is presently experimental and expensive. Only time will tell whether it becomes commonplace or not (or indeed, if it does, whether it's accurate enough to create active artificial proteins).

Fortunately, there is another alternative. We can combine existing protein chemistry with electronics to produce a hybrid technology. It is perfectly possible to produce protein molecules of various lengths and complexities in the lab (either through synthesis or the alteration of existing molecules). These may then be used in bioelectronic chips.

The idea is illustrated in figure 6. Here a protein is shown in-situ on a chip. It may be bound to the surface by electrostatic or other forces between its atoms and the chip pads or chemically by depositing an intermediate binding agent onto the pad surface. The geometry of the pad features ensures that the positioning is correct and different proteins can be assembled by adding them at different times and simultaneously placing the appropriate charges on the correct pads.

Figure 6. A hybrid electronic protein.



By monitoring the charge on the pads, their capacitance or other electrical parameters, we can discover if a molecule has bound to the active site. Similarly, by changing these, we could arrange to alter the configuration of a suitable protein to act like an enzyme - splitting or synthesising the attached molecules. This may need the addition of bound metal atoms to act as electron-carrying intermediaries in the system - a trick which nature herself uses in real proteins. Alternatively, the configuration of the protein could be changed by the binding of other “high energy” molecules like ATP. The simple formation of many thousands of pads and therefore sensors on a chip means that not all of them have to be successful for the chip to function. Different proteins could also be connected electrically together (through the wafer) in such a system – effectively making circuits or even logic gates (useful, for example, in checking if multiple proteins are present in a clinical situation or even acting like an artificial organ).

There are many obstacles to overcome before can finally fabricate such systems successfully. Apart from the fabrication of the silicon and the synthesis of the proteins, we also have to provide an on-chip environment to ensure that the organic molecules stay in one piece once assembled. This means a pH, contaminant and temperature controlled environment - a real challenge for the designer. However, the various pieces of technology are now in place to start experimenting with such systems.

Applications

The applications of such systems are almost endless. Perhaps one of the most obvious is in sensing. If we can synthesise binding sites for different chemicals we can detect their presence by measuring changes at the anchoring pads. In theory this would allow us to sense the presence of substances at the molecular level. Obviously such sensors could have many applications in environmental monitoring and medicine, particularly in the interface between man and machine.

A step beyond this is changing the configuration of the polypeptides by changing the electrical conditions at the pads or by bonding another chemical to the system. An application is the breakdown of unwanted substances into shorter chains. In this case the substance binds to the assembly and a change in configuration brought about by changing the charge on the pads or binding rips it apart as explained above. The

elimination of pollutants and production of hydrogen and oxygen from water are two examples. Synthesis is the opposite of this and is probably more difficult to achieve. However, it's also the application with probably the most potential. It could allow us to make artificial versions of natural materials which are currently beyond our capabilities like skin or spider's silk (which is incredibly strong).

In the longer term, perhaps the power of ATP or similar "high energy" molecules could be harnessed to produce power for small machines in an analogous way to its use in living organisms, for example by "burning" carbohydrates. One can even envisage a time when we abandon the clumsy internal combustion engine for more biological forms of power (engines might end up looking more like bagpipes). After all, if a horse can get through the day on a few mouthfuls of oats and a human on a plateful of sandwiches, why can't we devise engines similarly capable? In the very long term even systems like fusion power might yield to a similar approach.

The final application worth mentioning is the manipulation of DNA itself (as well as the other chemicals of life). This could allow us to sequence and analyse DNA on-chip and perhaps, in the long term, even synthesise custom drugs in the surgery - but that's the start of a whole other story.