Abstract – Manchester Association of Engineers, Dec 7th 2006

Dr. Henry Charlton

From Brewing to Biotechnology – The Evolution of a New Industry

Humanity has a history of exploiting biological systems for their own ends - fermentation of yeast in the absence of oxygen to produce alcohol being a widely known example.

As scientific theories superseded empirical approaches, vaccines and medicines were developed on the basis of using a biological system to generate these products. Such activity enabled the eradication of smallpox and the control of illnesses such as polio. Edward Jenner pioneered the application of cowpox infections to humans, which enabled eradication of smallpox, albeit almost two centuries later. With advances in our scientific understanding, vaccines against agents such as polio were also developed but the key difference between this and earlier vaccines was a scientific understanding of viruses and how to grow as well as harvest them for use in vaccines.

With the discovery of the structure of DNA and the means to manipulate it, new avenues of therapy, and indeed scientific advancement were possible. Areas of biotechnology (biotechnology meaning the commercial application of DNA manipulation techniques that were pioneered in the 1970s) include transgenic animals, gene therapy and genetic modification of plants for agricultural purposes.

However, a major part of the biotechnology industry can be represented by a number of "blockbuster" pharmaceutical products - all currently based on biologically active proteins. The volumes involved in this industry are very small compared to other multi-billion dollar industries – 100 kg of a drug substance might constitute the quantity required for a year of sales. Most of these drugs fall under the category of “monoclonal antibodies” which exploit the bodies immune system to destroy disease state entities, such as cancer cells.

Monoclonal antibodies are proteins, and the synthesis of all proteins is directed by genes encoded in the structure of DNA. Humanity’s ability to manipulate the structure of DNA, and insert it into various types of cell means that a wide range of proteins can be produced by “fermentation” or “cell culture” of the cells which have been modified. Mammalian cells tend to grow slowly in expensive growth media whereas bacteria grow quickly in inexpensive media. However, mammalian cells can produce larger, more complex, often readily active proteins whereas bacterial proteins tend to be smaller, requiring further steps to make their proteins active. Purification of these proteins typically then proceeds using technologies such as solid phase adsorption (chromatography – affinity, hydrophobic or ion-exchange), membrane based processes or filtration.

The structure of DNA itself is key to understanding developments in biotechnology. DNA is a polymer consisting of alternating phosphate and 5-carbon sugar residues, with constitute the poly-phosphate backbone of the molecule. Nitrogenous bases are bound to the sugar molecule and face an opposite and complementary strand of DNA. The sequence of just 4 bases makes up the code within DNA, and a sequence of 3 consecutive bases will determine the location and type of amino acid in a protein molecule. Hence, the ability to engineer DNA molecules facilitates the ability to manufacture proteins of choice.