

## 1.1 The element content of living systems

### 1.1.1 The biological elements

The analytical element content of cells as we know them today is in some way related to the limitations imposed by the genome, DNA, of the cell. However, the chemistry of a cell including the functioning of DNA and its synthesis only operates in a particular ionic medium and using a particular set of some accumulated twenty elements. Each cell also needs to collect energy. Hence, survival of a cell line, an organism, depends not just on reproducing DNA but on the uptake and use of selected elements and energy, all three being in a feed-back relationship. In fact, historically, DNA, or any other coded set of instructions such as RNA, could only have been an extra way of supporting and reproducing patterns of chemical reactions which predated it. The feed-back connection between DNA and the element content is brought about by proteins. It is then possible to describe a cell in terms of composition in at least three related and dependent ways: by its *genome* (DNA), by its proteins, a cell's *proteome*, and by its element content, which we may refer to as the cells' *metallome*. Other possibilities will be described later. In this book the approach to life starts from the simplest of the three, the element content, and then progresses to the more chemically complicated components and processes while stress remains on those molecular units which can be grouped together by their selected inorganic element content. The relationship to the genome and consequently to biological speciation will become clear later.

There are now known to be almost two million different 'species' of living organisms on earth (see Aside) and besides their phenotypic and phylogenetical characteristics we need to know their chemical similarities and differences to be able to understand what life is and how it works. An obvious start is the identification of the 'biological' elements. Analyses of many bacteria, a few hundred plant species, among the known 0.4 million, and of about two hundred among the catalogued 1.1 million animal species as well as of organs, tissues, and other substances of biological origin, have enabled us to establish the number and identity of the chemical elements present in biological systems and to recognize those that are 'essential' for bacterial, plant, and animal life. It became clear in these and related studies that, amongst the chemical elements, all biological systems concentrate certain elements while rejecting others and that some of the processes involved require energy. One could, therefore, speak of a natural selection of the chemical elements by biological systems, which involves a readjustment of the element distribution on the earth's local scale by utilizing energy ultimately provided by the sun.

## THE PROTEINS

The proteins are the third class of macrocomponents of living systems, and therefore of foodstuffs, that we are to consider.<sup>1</sup> Proteins are polymers with molecular weights ranging from around 10 000 to several million and are often described as having a highly complex structure. In actual fact there is a great deal about the structure of proteins that is quite straightforward. The monomeric units of which they are composed, the amino acids, are linked together by a single type of bond, the peptide bond, and the range of different amino acids is both limited in number and essentially common to all proteins. Furthermore, the polypeptide chain of proteins is never branched.

The special character of proteins lies in the subtlety and diversity of the variations, both in structure and function, which Nature works on this simple theme. The properties and functions of a particular type of protein depend entirely on the precise sequence of its amino acids, unique to that protein. Unlike the polysaccharides, there cannot be anything vague about the exact length of the chain. If even one amino acid in the sequence is out of place, then it is quite likely that the protein will lose its biological activity. It is the sequences of the amino acids in proteins which are defined by the sequences of bases in the DNA that make up our genes. The amino acid sequence of a protein, in this case the  $\beta$ -lactoglobulin of cow's milk, is shown in Figure 5.1. Although in some respects typical, this protein has been selected for illustration

$NH_2$ –Glu–Gln–Leu–Thr–Lys–Cys–Glu–Val–Phe–Arg–Glu–Leu–Lys–Asp–Leu–Lys–  
Gly–Tyr–Gly–Gly–Val–Ser–Leu–Pro–Glu–Trp–Val–Cys–Thr–Thr–Phe–His–Thr–  
Ser–Gly–Tyr–Asp–Thr–Glu–Ala–Ile–Val–Glu–Asn–Asn–Gln–Ser–Thr–Asp–Tyr–  
Gly–Leu–Phe–Gln–Ile–Asn–Asn–Lys–Ile–Trp–Cys–Lys–Asn–Asp–Gln–Asp–  
Pro–His–Ser–Ser–Asn–Ile–Cys–Asn–Ile–Ser–Cys–Asp–Lys–Phe–Leu–Asn–  
Asn–Asp–Leu–Thr–Asn–Asn–Ile–Met–Cys–Val–Lys–Lys–Ile–Leu–Asp–Lys–  
Val–Gly–Ile–Asn–Tyr–Trp–Leu–Ala–His–Lys–Ala–Leu–Cys–Ser–Glu–Lys–Leu–  
Asp–Gln–Trp–Leu–Cys–Glu–Lys–Leu–*COOH*

**Figure 5.1** The amino acid sequence of bovine  $\beta$ -lactoglobulin, one of the principal whey proteins. The standard three-letter codes shown in Figure 5.2, below, are used. The start and finish of the sequence are known as the amino ( $NH_2$ ) and carboxyl ( $COOH$ ) ends, respectively. The use of these terms is explained in Figure 5.3.

solely because its unusually small size makes it easier to fit on the page. Most proteins have polypeptide chains many times this length. Sequences such as these may appear random, but are in fact very tightly controlled and reproduced exactly in every molecule of the protein synthesised by a particular organism. With possibly only a few changes the sequence will normally be reproduced in related species, and often in much larger taxonomic groups.

As we will see later in this chapter, the proportions of the various amino acids in the proteins we consume are very important, but the total quantity is also at least as important. Table 5.1 lists the protein content of a wide variety of different foodstuffs.

## Clusters and their benefits

“Clustering” refers to local concentrations of horizontally or vertically linked firms that specialise in related lines of business together with supporting organisations, though definitions as to what exactly constitutes a cluster vary greatly. In this publication, concepts such as industrial districts, local production systems and regional clusters of innovation are used interchangeably and are commonly referred to as clusters for the sake of simplification. Even though above concepts highlight or emphasise slightly different cluster aspects, their main theoretical building blocks, namely agglomeration economies, endogenous development theory and systems of innovation overlap (Moulaert and Sekia, 2003).

Clusters allow enterprises to thrive under conditions of increasingly global competition. By clustering together, firms can achieve economies of scale and scope and lower their transaction costs due to geographical proximity and increased interaction often based on trust. Industry concentrations can lead to the appearance of localisation economies reducing costs through the availability of specialised labour and business services, public sector investments aimed at satisfying particular industry needs, as well as financial markets geared towards satisfying cluster firms’ demands. Clusters have also been identified as motors for innovation, as companies co-operating and competing at close geographic proximity can learn from each other, developing unique local knowledge and creating knowledge spill-overs in the process. The introduction of new technologies is favoured both by the element of competition, as well as by the possibility

of cost-sharing among cluster participants. Competitive advantage commonly associated with clusters does not limit itself to firms participating in a cluster it also benefits the whole regional economy where a cluster is located.

Clusters are an international phenomenon that exists in a multitude of shapes and sizes. A cluster can contain a small or large number of enterprises, as well as small and large firms in different ratios. Clusters can consist exclusively of firms operating in the same line of business or include whole supply and value chains. Clusters vary widely regarding the number of participants and their degree of organisation. For example, they generally contain firms that compete against each other, although co-operation may be achieved on a case-by-case basis. In some cases, inter-firm networking leads to the creation of strong horizontal bonds among firms supported by social institutions, whereas in others, vertical links with very little interaction and no cluster organisational sub-structure may prevail. How far a cluster may geographically expand is a topic of debate. Depending on the individual cluster logic, a cluster may be firmly rooted in a local context or indeed span a whole country with cross-border or international links. Clustering occurs in all branches of industry, be it high-tech or traditional industries, as well as in agriculture or in the service sector with each cluster being a unique constellation in time and space.

## 19 Management of Recalcitrant Chronic Rhinosinusitis Following Endoscopic Sinus Surgery

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Chronic rhinosinusitis (CRS) is a chronic sinonasal inflammatory mucosal disease that responds well to both medical and surgical management in the majority of patients. It is one of the most common chronic diseases in the US population, affecting up to 14% of the adult population. Patients with CRS who fail maximal medical therapy are candidates for endoscopic sinus surgery (ESS). Patients undergoing ESS should be counseled that surgery is not a panacea, and continued long-term medical therapy in the form of both topical and systemic anti-inflammatory and/or antimicrobial medications is likely necessary. Many otorhinolaryngologists, however, have encountered patients who continue to suffer from severe symptoms of CRS following appropriate ESS despite continued “standard” maximal medical therapy in the form of routine nasal saline irrigations, topical nasal steroids, leukotriene inhibitors, allergy therapy, and appropriate courses of systemic steroids and antibiotics, when indicated.<sup>1</sup> This subset of patients may relapse quickly with frequent exacerbations despite optimal ESS and optimal standard medical therapy. This relatively small, yet challenging, patient population poses a significant and often frustrating dilemma to the rhinologic surgeon. To date, there is no consensus regarding the optimal treatment of this subset of patients suffering from recalcitrant CRS.

CRS is widely accepted to be a multifactorial disease with no definitively proven single etiology. A common underlying factor in all cases of CRS, however, is chronic sinonasal mucosal inflammation. Several etiologies for chronic mucosal inflammation have been proposed, including chronic bacterial infection, allergy, immune dysregulation, biofilms, fungus, superantigen production, ciliary dysfunction, and immunoglobulin deficiency, among others. Therapies for CRS are directed at reducing sinonasal inflammation at various points along the inflammatory cascade while simultaneously eliminating or controlling the underlying source of the inflammation. Inflammation and edema of the sinonasal mucosa leads to ostial occlusion and subsequent hypoxia within the occluded sinus. This leads to goblet cell hyperplasia, increased mucus viscosity, and the accumulation of thick, sticky mucus within the sinus resulting from impaired mucociliary clearance. Mycostasis provides an opportunity for bacterial overgrowth and chronic bacterial infection within the sinonasal cavities, which summons further inflammation due to intrinsic host defense factors.

### *The Totality of Intellectual Rituals and Sacred Objects*

The intellectual world consists of all the interaction rituals which take place periodically across the landscape and of the flow of sacred objects—ideas and texts—which result from them. To envision the intellectual world this way is deliberately to challenge our prevailing conceptions of intellectual life, whether contemporary or historical. When we ourselves formulate “what is happening” in the intellectual world, we invariably impose an image of one or a few currents, typically distorted by partisanship. Intellectual historians may be less partisan because of greater distance, but their view remains partial, fitted around a few patterns and necessarily limited to a manageable number of names and themes. But the intellectual world is much bigger than that, and not so tightly focused. The most detailed evidence we have covers natural scientists, who make up only part of the intellectual world. In the 1970s there were approximately 1 million natural scientists publishing in any year and 110,000 social scientists (Price, 1986: 234).<sup>11</sup> If we go backwards in history,

or laterally into less active fields, the numbers are smaller, but in every case the total active intellectual community is much bigger, and more diverse, than the simplified pictures that even the most assiduously detailed history presents. And even this is not far enough. Intellectual activity is intermittent. Today there are more than a million scientists who come in and out of activity every few years; the mass of the scientific community is in this intermittent class. Still larger is the surrounding fringe of students, would-be intellectuals, vicarious participants, intellectuals in transition in or out. This is the reality on which we impose our simplifications.

Imagine what it would be like to see through walls and even into people’s minds. The social landscape would appear to us flickering with thoughts. If one walked everywhere throughout the corridors of a large university, hearing lectures and conversations and the inner conversations that constitute thinking, one’s sensation would be of tremendous variety, even cacophony. There would be plenty of mundane, non-intellectual thoughts: people thinking about tasks they have to do, ruminating about their friends and enemies, plotting erotic or organizational politics; bitter obsessive thoughts, perhaps some rehearsing of lines and replaying of jokes, as well as scattered bits of words, phrases, images, the flotsam and jetsam of recent past exchanges of cultural capital. But some of these ideas would be glowing brightly with emotional significance, charged up by interaction rituals into sacred objects. These are the ideas that act as magnetic poles in intellectual thinking, that are the focus of the long and serious attention that is the activity of the intellectual world at its most intense.

## 2. Cutting

### a. General Aspects

Cutting is applied to ductile, viscoelastic, and elastic materials. Products of cutting are large pieces (e.g., meat), slices, diced products (e.g., small cubes of fruits), flakes, and pulps. The main forces exercised are shear forces. Distinction is made between cutting up and dissecting. Methods of cutting up are slicing and dicing, while examples of dissecting are shredding and carving. Cutting of food is performed by knives, saws, shears, and thin wires. Table 4-2 presents a classification of cutting equipment and tools. The selection of the right cutting tool depends on the product, its condition (e.g., fresh or processed), and the desired quality of the cut. Knives and other cutting tools can be portable for manual use, or they may be part of machines.

The factors influencing cutting depend on the method applied. Although there is a great difference between manual and automatic cutting, some factors influence both kinds of cutting, such as (1) product to be cut; (2) sharpness of cutting tool; (3) cutting force; (4) direction of force applied; and (5) cutting speed.

Advantages of cutting processes are: (1) wide product range of application (from meters to micrometers); (2) increasing the value added; (3) removing of spoiled parts; and (4) screening out of undesired material that otherwise would burden processing.

Disadvantages of cutting processes are: (1) large differentiation of required equipment; (2) personnel must be skilled; (3) production per employee is low; (4) high safety requirements; and (5) frequent wear out of cutting tools.

Cutting entails a relative motion between cutting tool and product. There are two main possibilities: (1) the cutting tool is fixed, while the product moves toward the tool; and (2) the cutting tool moves toward the fixed product that is to be cut. In some cases, both tool and product move in counterdirection, increasing cutting effectiveness.

Basic element of almost all cutting equipment are the knives. When a knife cuts, two zones near the cutting edge are distinguished, the zone of plastic deformation, which lies directly on the cutting edge, and the zone of elastic deformation, which lies between the previous zone and the product (Fig. 4-3a). The effectiveness of cutting depends on the cutting edge of a knife and the "cutting angle"  $\lambda$ , which is the inclination between the knife axis and the perpendicular to the cutting direction

(Fig. 4-3b) (Tscheuschner, 1986). Factors influencing the cutting edge are: the quality/hardness of metal, the fineness (width,  $s$ ) of cutting blade, and the wedge angle,  $\alpha$  (Fig. 4-3c). The finer a cutting blade and the narrower a wedge angle, the finer is the cut. Nevertheless, due to strength and wear limits, there are also limits to the reduction of the width of knife blade, and to the angle of its wedge.

Figure 4-4 indicates the forces exercised during cutting by a straight knife and by a rotating disk knife. The force  $F$  during cutting depends on the normal force ( $F_N$ ), the tangential force ( $F_T$ ), and the cutting angle  $\lambda$ .

$$F = (F_N^2 + F_T^2)^{1/2} \quad (4.1)$$

## **Viruses, “At the Edge of Life”**

The unicellular *microorganisms* can be arranged in order of decreasing size and complexity: protozoa, fungi, and bacteria (the latter including mycoplasmas, rickettsiae, and chlamydiae). These microorganisms, however small and simple, are *cells*. They contain DNA as the repository of their genetic information; they also contain RNAs and they have most or all of their own machinery for producing energy and macromolecules. These microorganisms grow by synthesizing their own macromolecular constituents (nucleic acids, proteins, carbohydrates, and lipids), and most multiply by binary fission.

Viruses, however, are not cells, are not microorganisms. They possess no functional organelles and are completely dependent on their host for the machinery of energy production and synthesis of macromolecules.

They contain only one type of functional nucleic acid, either DNA or RNA, never both, and they differ from microorganisms in having two clearly defined phases in their life cycle. Outside their host cell, the viruses are metabolically inert; this is the phase of their life cycle involved in transmission. Inside their host cell, the viruses are metabolically active; this is their replicative phase in which the viral genome exploits the machinery of the host cell to produce progeny genome copies, viral messenger RNA, and viral proteins (often along with carbohydrates and lipids) that assemble to form new virions (*virion*, the complete virus particle). Unlike any microorganism, many viruses can reproduce even if only their genomic DNA or RNA is introduced into the host cell. These qualities have been used to argue the question, "Are viruses alive?" One answer is to envision "*viruses, at the edge of life,*" in some ways fulfilling the criteria we use to define life, in some ways not. The key differences between viruses and microorganisms are listed in Table 1.1.

Given their unique characteristics, where might viruses have originated? There are two theories that have been argued for many years: viruses are either degenerate bacteria that have lost most of their cellular functions or they are escaped eukaryotic genes, i.e., nucleic acids that have learned to survive outside the environment of the cell. Viral genomic sequence analyses may at last resolve this question: for example, the genome of a plant viroid (a subviral agent composed of naked RNA), potato spindle tuber viroid, seems to be a self-replicating RNA copy of a bit of host DNA. Many of the genes of poxviruses are similar to those of eukaryotes. In any case, it seems certain from viral genomic sequence analyses that all the viruses did not evolve from a single progenitor; rather the different kinds of viruses likely arose independently and then continued to diversify and adapt their survival and transmission qualities to better fit particular niches by the usual Darwinian mutation/selection mechanisms. Some viruses have continued to evolve in long association with their evolving hosts (e.g., the herpesviruses); others have evolved by "host species jumping" (e.g., influenza viruses) and yet others by developing zoonotic transmission schemes (e.g., rabies virus).