First Signals: The Evolution of Multicellular Development. John Tyler Bonner. Princeton University Press, 41 William Street, Princeton, New Jersey 08540, USA. 2000. 146 pp. Price: US$ 19.95/£12.95.

The major focus of present-day developmental biology is the understanding of the fundamental principles that guide a single cell, the fertilized egg, to develop into a complex multicellular organism with form and pattern. The combined approach of using genetic and molecular methods has produced an explosive burst of knowledge that has extended our understanding of developmental mechanisms at the molecular level. Nonetheless, in biology, everything makes sense only from the point of view of evolution. Developmental biology is no exception to this – understanding the evolution of developmental mechanisms is central to our understanding development. In this context, an even more challenging problem is understanding the evolution of multicellularity itself, the transition from being an organism with a single cell to one with many cells. Undoubtedly, this is a significant step in evolution leading to biological diversity. This delightful and thought-provoking book *First Signals* by John Tyler Bonner makes an attempt at the monumental task of understanding the evolution of multicellularity. Like the pioneering experimental work of the author, the book is also elegant in the simplicity of approach and the breadth of the questions it poses. The book's apparent simplicity is deceptive though, as it takes us through the complex conceptual issues of multicellular development. It strikes a fine balance between three approaches that have been used to understand development: the largely descriptive classical approach, the reductionistic approach of the molecular biologist, and the theoretical approach that involves mathematical model-building. The fact that it is a personal narrative, highlighting the historical events in the evolution of developmental biology as a discipline, makes it highly readable. In the author's words, it is a search for a 'simplicity theory' for a complex phenomenon.

The emergence of multicellularity was an important transition point in evolution. From the point of natural selection, this resulted in a shift from a single cell being the unit of selection, to a group of cells as a unit on which natural selection could act. What could be the factors that influenced selection of a group of cells versus a single cell? Size of the unit is an important factor that can influence selection. Bonner's own view is that 'the first step was a size increase due to an accident, for instance, a mutation that prevented daughter cells from separating. If the larger cell mass has any advantage, such as producing a protected internal environment, then natural selection will see to it that the novelty is retained'. This major theme is examined in detail throughout the book. What follows is a lucid synthesis of ideas, some old and some new.

An examination of the life cycles of terrestrial and aquatic organisms suggests two broad possibilities for the origin of multicellularity. 'All aquatic organisms (probably) began their multicellularity when the products of cell division failed to separate, while most terrestrial microorganisms involved motile aggregation of cells or nuclei in a multinucleate syncytium'. The author concedes that, in the case of microorganisms, it is difficult to make a clear distinction between aquatic and terrestrial forms, as most microorganisms probably go through both phases in their life. Another important point about multicellularity that has been emphasized is that it arose at different points of time in evolution in different organisms. This again reinforces the idea that there has been significant selection for it. Two major advantages of the size increase that accompanies multicelluarity that have been emphasized are that it helps in feeding and also prevents from being eaten by predators. What is interesting is that the multicellular organism has to revert to a unicellular phase for reproduction.

What could be the mechanisms that prompted terrestrial cells to aggregate and flock together? The roots of the issue of multicellular development lie in the answer to this fundamental question. This takes us directly to the central theme of the book, the first signals that brought cells together. Without doubt, one is entering the realm of speculation. For the process of aggregation to be efficient, the generation and reception of signals between cells have to be integrated. Undoubtedly, the environment must also have provided some of the early signals. The evolution of the signal–response system is therefore crucial in deciding as to how the cells respond among themselves and also how the organism communicates with other members and the environment. Though signal transduction has now been recognized as an important biological process, very little information is currently available on the cellular signalling systems that were present in the early stages of evolution. Bonner takes us through the land of primordial signal molecules and morphogens. He draws an interesting parallel between cellular signalling and the behaviour of social insects. An important aspect of signalling that becomes apparent is that the signals and the receptors must have co-evolved.

The next most important conceptual issue in understanding development is the origin of polarity. Polarity is the first cue that initiates the formation of complex patterns. Asymmetry is also central to unicellular development. Considerable attention has been devoted to the generation of asymmetry during development by molecular biologists in the recent years. The problem has been reduced to one of asymmetric protein localization in the cell. Many developmental processes such as sporulation in bacillus species and differentiation in *Caulobacter* involve generation of asymmetry by differential localization of specific proteins and regulators within the cell. Similarly, asymmetrically-distributed morphogens direct pattern formation in more complex multicellular organisms. However, this only pushes the problem back by one step; the localization of the morphogen or regulator has to follow some environmental cue. The basic mechanism of asymmetric localization of proteins, though models abound, remains a central problem in developmental biology. Bonner's attempt to address this issue is to take us through the life cycles of several unicellular and multicellular organisms and examine the environmental cues that generate polarity. This culminates with the examination of the slime moulds, one of the prominent models of developmental biologists and the author's own favourite system. Bonner discusses the classic experiments that illustrate the different conceptual issues discussed in the previous chapters. This includes development in

one-dimension in a capillary and in two-dimensions in a monolayer of cells, both pioneered in the author's laboratory. The result is a blend of the macroscopic, microscopic and molecular views of development. Taking us through the fascinating molecular studies on development, Bonner compares this to 'following a rainbow at breakneck speed looking for the pot of gold at the end'. While acknowledging the immense contributions of the molecular studies, he cautions us that the 'search for gold may involve an infinity of regressions'. So what is the solution? The best is an integration that brings together different approaches and ideas, including mathematical models, that address the central issues of development. The bottom line is, we are trying to understand what happened millions of years ago by studying organisms that have gone through the process of natural selection, time after time. In this connection, the mathematical models help us strip the inherent complexity and redundancy present in living systems that have become complex over the years.

In summary, in a world that is exploding with information, generated predominantly by the reductionistic approach of molecular biology, Bonner's book helps us to keep in perspective the fundamental conceptual issues of multicellular development. The book's message is that initially, there was a selection for larger size, easily achieved by multicellularity. The evolution of signal-receptor systems helped the maintenance of the multicellular state by a process of integration. Subsequently, efficiency was achieved by cell differentiation, aided primarily by the polarity conferred by the environment. The multicellular organisms of today are the ones that have successfully gone through these processes several times in evolution. This simple message will appeal to both professional developmental biologists as well as students of biology initiating their study of development.

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A Treatise on Fluorosis. A. K. Susheela. 2001. 119 pp. Price: Rs 300.

In *A Treatise on Fluorosis*, A. K. Susheela emphasizes the toxic effects of excessive fluoride ingestion. Skeletal fluorosis, dental fluorosis and non-skeletal fluorosis, like the involvement of skeletal muscles, red blood cells and gastrointestinal tract are highlighted and their differential diagnosis is discussed in detail. Early examination methods are suggested and the book is illustrated with detailed case reports of toxic fluorosis. The tables and illustrations are clear, the book is student-friendly and made easy to read. Prevention of fluorosis with special reference to proper diet is very well brought out. The recipes given seem to be well tried-out. Screening tests recommended are practical and useful.

A statement appears in the book (p. 60) that 'dental caries has no correlation with water fluoride content' and again 'fluorosis occurs even with 0.6 mg/l of fluoride in drinking water' as shown in a study in Machgar village. This statement is made on the basis of an MDS thesis by Gajender Singh Meena in 1983. This is however debatable. In 1901, Fredrick McKay (*Dent. Cormos*, 1916, **58**, 477–484) of Colorado, USA noted that many of his patients had permanent stains on their teeth. These brown stains were related subsequently to the presence of fluoride in the drinking water. Systemic investigations by Dean *et al.* (*Public Health Rep.*, 1931, **54**, 852–888) from 1920 to 1936 concluded that water containing 1 ppm fluoride had maximum cariostatic effect. This led to a major breakthrough in preventive dentistry.

In spite of the abundance of data on the role of fluoride as a most safe, economical and effective tool for prevention of dental caries, controversies erupt from time to time throughout the world and the scenario in India is no different. Its safety has been repeatedly established and a voluminous literature exists on this subject. The Federal Register of US Food and Drug Administration has declared fluoride as an essential nutrient for human health and the WHO expert committee (WHO Tech. Rep. Series No. 532.5, 1977) on trace elements in human health also includes fluoride among 14 trace elements essential for the normal growth and development of human health.

So convincing has been the effect of water fluoridation as a public health measure to curb dental caries that by mid-1980s, approximately half of the population of USA (105 million) was consuming optimally fluoridated water. Approximately 60 million people in 40 countries elsewhere are protected by artificial fluoridation.

In India, 5% of the population lives in endemic fluoridated areas and another 3% in optimal fluoride areas (Tewari, Amrit, *J. Indian Dent. Assoc.*, 1986, pp. 9–10). Thus, 85–90% of the population lives in fluoride-deficient areas. Systemic research in the various physiological, metabolic and toxic aspects of fluoride reveals that 1 ppm of fluoride in drinking water has no biological side effects on the vital organs of the human body. Observations in endemic fluorosis areas reveal that fluoride up to 4 ppm in drinking water produces skeletal fluorosis and above 8 ppm, coupled with malnutrition, causes not only skeletal fluorosis but also irreversible bony changes and deformities.

Therefore, in the human system fluorides have a dual role, i.e. a harmful effect above 4 ppm and a caries-preventive and health-promoting effect at 1 ppm.

Susheela's treatise deals only with the toxic effects of fluoride. It is however necessary to balance this against the merits of controlled fluoridation of water supply for the prevention of dental caries. The book will appeal to all students of dentistry and dental practitioners.

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