Molecular Genetics of Bacterial Pathogenesis: A Tribute to Stanley Falkow. Miller, V. L., Kaper, J. B., Portnoy, D. A. and Isberg, R. R. (eds). American Society for Microbiology, ASM Press, Washington, DC 20005, USA. 1994. XL + 529 pp. Price: £ 59.50.

This volume is meant to commemorate the 60th birthday of Stanley Falkow, who, with his enunciation of 'molecular koch's postulates', laid the foundations of molecular genetic analysis of bacterial pathogens. 'Legacy of Stanley Falkow' by Kaper and Miller brings out his extraordinary talents as a researcher matched by his exceptional skills as a teacher. In 'A look through retroscope' Falkow himself recounts the origins of his interests in bacterial pathogenicity, which started after reading *Microbe Hunters* at a very young age, and culminated in unravelling several of the molecular underpinnings of bacterial pathogenicity.

The main text of the book is divided into six parts.

Part I – 'Retrospective look at early advances' – is a historical account of how Falkow's work on extrachromosomal elements, especially R factor, increased the awareness of the scientific community that plasmids were not a curiosity of geneticists but rather had far-reaching practical implications, viz. role in bacterial pathogenesis and antibiotic resistance (Chapters 1, 2). There are reviews on the role of Tn3 in the spread of antibiotic resistance (Chapters 3, 4) and application of plasmid profile analysis to trace the epidemiology of pathogenic bacteria, which is now a burgeoning field of 'molecular epidemiology' (Chapter 5).

Colonization of the host surfaces by pathogenic bacteria represents the first and an almost indispensable step in the initiation of infectious disease process. Thus, an interest in colonization factors, both for studying the bacterial pathogenicity and for designing interventional strategies, cannot be overemphasized. Part 2 – 'Adhesins' – discusses molecular genetics of an array of colonization factors, viz. adherence factors of urinary tract pathogens (Chapter 6), *E. coli* type 1 pili (Chapter 7), pilus antigenic variation (Chapter 8) and type 4 pili (Chapter 9). These chapters not only depict the state-of-the-art of the subject but also relate the chequered path of the development of each of these areas.

Until recently, adhesins were seen as appendages passively mediating attachment of pathogens to single receptor on the host or target cells. It is, however, becoming clear that adhesins are much more complex structures in having multiple binding sites and their function is not limited to passive binding but extends to signal transduction in host/target cells. To carry out such functions adhesins mimic host molecules whose natural functions involve adherence and signal transduction. Also, co-operation exists between different adhesins in establishing an infection which is reflected in the organization and regulation of their genes. These aspects have been discussed in relation to adhesins of *Bordetella pertussis* (Chapter 10), *Haemophilus influenzae* (Chapter 11) and E-PEC (Chapter 12). Discussion on murine colonic hyperplasia, a naturally occurring disease of mice caused by *Citrobacter freundii* biotype 4280, has obvious relevance to the study of human proliferative bowel disorders (Chapter 13).

Intracellular bacteria, whether obligate or facultative, present enormous challenges to scientific and medical community. Part 3 – 'Molecular and cellular biology of intracellular bacteria' – present a detailed account of the molecular underpinnings of virulence determinants of intracellular bacteria and the cell biology of their interaction with host cells. Exhaustive genetic approaches have been used to identify *Salmonella* virulence genes. The various genes under investigation are: *spv* (*S*almonella *p*lasmid *v*irulence), *spa* (*s*urface *p*resentation of *a*ntigen), *inv* (*inv*asion), *pag* (*Pho-P a*ctivating *g*enes) (Chapter 14). Spectacular events in the host cell which accompany the invasion of *Yersinia* (Chapter 15) and *Salmonella* (Chapter 16) into the cell are also discussed.

Studies on the molecular aspects of the growth of *Legionella pneumophila* within the phagocytic cells have been presented to provide a comprehensive model by which pathogens may manipulate the host cells to suit to their intracellular lifestyle (Chapter 17). The host response to *Listeria monocytogenes*, an important food-borne pathogen, has been reviewed as a paradigm of cellular immune response to intracellular pathogens (Chapter 18). The emphasis of the review is on the cell biology of this infection, i.e. pathogen's entry into the host cell, its escape from the phagocytic vacuole using listeriolysin O (LLO) and the role of actin-driven movement in intercellular spread. The molecular genetics of chlamydial pathogenesis are currently under intensive investigation. In this context, the recently proposed chlamydial adhesins, viz. major outer membrane protein (MOMP), chlamydial cytoadhesin (CCA), Hsp-70 and another outer membrane protein (omp-2) have been reviewed. The potentialities of some of these antigens for the development of a vaccine have also been discussed (Chapter 19).

Part 4 – 'Extracellular structures and products' (Chapters 20–26) – is a critical account of the molecular genetics of the most obvious virulence determinants, viz. capsules (*E. coli* K-1 and Group B streptococci – type III), toxins (pertussis toxin and *E. coli* verotoxins), *E. coli* hemolysin, flagella (*Campylobacter* spp.) and yops (*Yersinia* spp.). Detailed information on the molecular genetics of these products has been gained primarily because these virulence factors have been most amenable to tools of molecular biology. The biosynthesis and assembly of these virulence factors have been discussed in detail. The high degree of sequence and functional conservation among dispartate virulence factors has been summarized succinctly. In these chapters, some of the very interesting topics which provide newer leads for further research are: periplasmic space of gram negative bacteria as a potential target for antimicrobial agents, study of *E. coli* hemolysin in conjunction with lipopolysaccharide to unravel its exact role in pathogenesis and tyrosine phosphatase activity of the yops of pathogenic yersiniae and their homology to eukaryotic signal transduction proteins.

Part 5 – 'Virulence gene regulation' – discusses molecular genetic mechanisms underlying regulatory loops responsible for the expression and regulation of virulence genes. The complexity of these regulatory loops has been illustrated by the well-known *bvg* regulation in *Bordetella pertussis* (Chapter 27) and methylation-dependent and *Lrp* (*L*eucine *r*esponsive regulatory *p*rotein)-dependent fimbrial gene expression in *E. coli* (Chapter 28). In addition to these, two other systems, namely urease as a potent virulence factor (Chapter 29) and plas-

mid-mediated iron transport virulence system of *Vibrio anguillarum* (Chapter 30), have been discussed. The chapter on urease makes very interesting reading wherein genetic organization and regulation of urease genes of members of enterobacteriaceae (*Proteus mirabilis*, *Klebsiella aerogenes* and *E. coli*), gram positive bacteria (*Staphylococcus saprophyticus* and a thermophilic *Bacillus* sp.) and *Helicobacter pylori* have been discussed.

Part 6 – 'Other aspects of bacterial pathogenesis' – is an assemblage of assorted aspects of bacterial pathogenicity which arose during Falkow's work detailed in the preceding chapters. None of these topics have been dealt with in previous compilations on the subject. It is apparent that these aspects of bacterial pathogenicity would constitute important areas of research in the future.

The enzyme systems responsible for sucrose transport, sucrose hydrolysis and synthesis of extracellular and intracellular polymers have been viewed as pivotal virulence factors for the cariogenic *mutans* streptococci. Newer tools which may help elucidate molecular mechanisms underlying synthesis, regulation and interrelations of these enzymes have been discussed (Chapter 31).

In general, it is very well-known that several factors, both host and pathogen, determine the minimum inoculum required to produce a disease in susceptible hosts. In this regard genetic determinants of acid resistance of *Shigella* spp. have been discussed (Chapter 32). However, the thought-provoking question in this chapter is: Are there any specific factors which dictate infective dose of a pathogen?

A great deal of progress has been made in recent years in the field of mucosal vaccines. Various aspects of the subject discussed include – cholera toxin subunit B as a model for the development of nonliving mucosal vaccines, its use as an adjuvant for other mucosal vaccines and live mucosal vaccines as carriers of heterologous antigens (Chapter 33).

The discussion on phylogenetic diversity of microbial pathogens (Chapter 34) brings into focus the bias of *in vitro* growth enrichment methods towards bacteria isolated from the environment. To what extent are these methods relevant to microbial flora of mammals? The inadequacy of these methods has been illustrated by the identification of unculturable pathogens directly from host tissue using PCR-amplified 16S rRNA sequences.

Since this volume is meant to be a tribute to Stanley Falkow, all the contributors are his former students, postdoctoral fellows or collaborators. So only those aspects of bacterial pathogenicity which have been pursued in his laboratory are reviewed. Nevertheless, it encompasses not only a good range of microbial pathogens and virulence determinants but also incorporates certain aspects, especially in Part 6, hitherto not dealt with in any of the previous works on this subject.

The book has the characteristic stamp of the American Society for Microbiology, i.e. highly authoritative and immensely readable.

All in all, this volume should form an important part of any collection, whether individual or library, dealing with bacteriology, medical microbiology, bacterial pathogenesis or infectious diseases.

J. S. VIRDI

Department of Microbiology,
University of Delhi South Campus,
Benito Juarez Road,
New Delhi 110 021, India.

Life in Moving Fluids. Steven Vogel. Princeton University Press, 41, William Street, Princeton NJ 08540, USA. 1994. 2nd edn. 467 pp. Price: $ 49.50, £ 35.

Scientists of yesteryears were known as natural philosophers: people who wondered about the workings of Nature. They appear to us as free souls, knowing no boundaries of specializations, and venturing into any body of knowledge to seek an explanation to some riddle that caught their imagination. The book *Life in Moving Fluids* by Steven Vogel is a beautiful one, one that revives the memories of the natural philosopher. It is an account of a biologist stepping out of his customary confines and thinking about the effects of flow on life in moving fluids.

Fluid mechanics has become a subject highly mathematized with a quest for exact results. The advent of high-speed computers has only enhanced this trend, and the frontier is occupied by computations of creeping flows, direct numerical simulations of turbulent flows, etc. All this is not a criticism of what goes on in fluid mechanics, but one does wonder: Is there any room for natural philosophers in fluid mechanics? Vogel's answer is an emphatic yes.

The book is structured as follows: Each chapter begins with an introduction of a set of fluid-mechanical concepts, followed by the role they play in a wide variety of biological phenomena. The discussion is clear and simple, and the speculations are intriguing. The author also describes many simple experiments done by himself. The gentle humour which he employs in his exposition is a bonus.

The book begins with the notion of a fluid and that all important property – kinematic viscosity. Here we learn how viscosity plays an important role in the lives of antarctic mammals and birds, and affects the morphology of some microcrustacean species. Then follow the very important concepts of kinematics: conservation of mass and streamlines. Based on these simple ideas one can calculate the number of capillaries in our body, even without needing the proverbial back of an envelope. The next topics are pressure and momentum. A clean derivation of Bernoulli's equation, and nice examples of flow measurements are presented. The ideas of pressure distribution and lift forces follow naturally, giving rise to beautiful examples of how these principles are 'used' by organisms to generate secondary flows, e.g. by termites to ventilate their mounds. All this leads up to a discussion of Newton's second law. It is nicely tied up with jet propulsion. It is really incredible that many living beings move by this principle, and belong to the 'jet set'!

The next few chapters drag 'drag' into focus. The new player is the Reynolds number. Here the origin of the drag force, the vagaries of the drag coefficients, separation of flow, streamlining of shapes, and scale modelling are explained in a very clear manner. Some of the author's own clean and simple experiments on scale modelling are presented. Application of the principles of drag to biological systems leads to an immediate complication since the shapes of living things are flexible and hence can interactively change with flow. Thus, there can be no discussion of 'dragginess' of a shape. All these ideas are discussed in the context of trees, microalgae, motile animals, etc.,