

interest, among which a few are mentioned below. Leigh and Dodsworth (p. 349) review the central role of the PII proteins in sensing (indirectly) nitrogen limitation. Liande *et al.* (p. 423) describe the important roles of heterotrimeric G proteins in the growth and virulence of filamentous fungi. Mackenzie *et al.* (p. 283), based on the availability of genome sequence of and proteomic studies on *Rhodobacter sphaeroides*, present a case as to how such studies may shape future *R. sphaeroides* research. Drake and Horn (p. 169) describe the interactions of soil microorganisms with the earthworm gut and their impact on terrestrial nitrogen cycle. Overall, the editors have collated a diverse and a rich assortment of reviews, a must read for microbiologists. The exceptional organization of reference sections of the various reviews is another noteworthy feature.

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'The Annual Review of Physiology strives to bring molecular and mechanistic insights to problems concerning the physiology of the whole organism' – a goal that is currently known by somewhat trendier terms. The 2008 *Annual Reviews* exemplifies this approach in several reviews, notably those on obesity. Obesity with its implications for heart attacks, stroke, and diabetes is a problem that is growing as rapidly as the weight of the population. Understanding energy balance, feeding behaviour and weight reduction requires understanding mechanisms in both the central nervous system and peripheral mechanisms of monitoring and control. Sandoval *et al.* suggest that the remarkably precise balance maintained between caloric intake and expenditure may be mediated by signals for both glucose homeostasis and energy homeostasis converging onto the same region of

the hypothalamus. Both sets of signals modulate the same subset of pathways, leading to the precise balance.

Some of these pathways involve the use of  $\text{Ca}^{++}$  as a 'second messenger'. The central place of calcium in physiology can be discerned by the number of reviews devoted to processes involving calcium signalling. Donald Bers reviews signalling in cardiac myocytes, and points to the importance of considering integrative influences at the tissue and cellular levels of numerous individual molecular regulatory mechanisms – many involving calcium. Calcium currents underlie the upstroke of the action potential in pacemaker cells while the ion, either directly or through calmodulin or calmodulin-regulated kinases, modulates a range of other cardiac currents, including  $\text{K}^+$  and  $\text{Na}^+$  currents. And that is besides its role in excitation-contraction coupling. The authors highlight the complexity of the kinetics of exchange of  $\text{Ca}^{++}$  for  $\text{Na}^+$ , which is regulated by the thermodynamics of the rapidly changing ion gradients in the course of cardiac pumping. The exchanger (NCX) mediates both inward and outward fluxes during the same action potential, and also has roles to play in pacemaker function and in some arrhythmias, making it a transporter of some importance. Watch this space for a review of this antiporter in the not too distant future.

$\text{Ca}^{++}$  signalling is critical in life-and-death decisions for cells. Rong and Distelhorst review  $\text{Ca}^{++}$  signalling regulating Bcl2 family members and hence survival vs programmed cell death in T-cells of the immune system. While developing in the thymus these cells are exposed to a range of molecules made by the host organism. Strong activation of the developing T-cells causes sustained elevation of  $\text{Ca}^{++}$  levels in the cytosol and leads to death; weak activation results in oscillation of  $\text{Ca}^{++}$  concentration in the cytosol and leads to survival. This process serves to eliminate cells that would otherwise have gone on to mount an immune response against host molecules – as in auto-immune diseases. And selects for cells that are capable of mounting a response against foreign invaders. The mechanisms by which these responses are generated are discussed and shown to operate in other systems as well, including a form of cell death in the nervous system that is responsible for some types of neurodegenerative disease.

Yet another review emphasizing precise control of  $\text{Ca}^{++}$  transients is that by Kaupp and co-workers on sperm chemotaxis. Sperm can respond to almost homeopathically low (femtomolar) concentrations of the chemoattractant resact and its response has a dynamic range spanning six orders of magnitude. Here again the authors suggest calcium waves underlying the response, and trace a pathway for generating such waves. Essentially the system responds to changes in concentration rather than the concentration itself, i.e. a temporal as opposed to spatial sampling. The parallels with bacterial chemotaxis are striking. The authors, one of whom first cloned genes for the cyclic nucleotide gated channels involved in vertebrate vision, compare sensory transduction in the olfactory and visual systems to sperm chemotaxis. They suggest that sperm also responds to single molecules of attractants much as a photoreceptor can respond to a single photon of absorbed light.

Signalling is critical in physiology and this volume introduces a relatively new receptor for estrogen. Prossnitz and co-workers inform us that estrogen operates through the classical nuclear receptor for steroid hormones, but also signals through a receptor based in the plasma or cell membrane. The existence of the latter had been speculated in the 1990s. The membrane receptor was first identified in 2000 and falls into a well-known class of receptors – those that pass on the extracellular signal to a G-protein, which amplifies and passes on the signal to initiate a cascade of phosphorylation steps in the cell. Traditionally, incoming signals were presumed to either use this cascade approach or to actually enter the cell and proceed to the nucleus where they affected the expression of specific genes. Apparently estrogen does both (possibly through both sets of receptors) and this may have implications to the formation and possible targetting of hormonally regulated cancers.

A place where one does not normally associate such fine-tuned signalling is in the mucous layer of airways – a place traditionally associated with gas exchange but contaminated with inhaled microorganisms, particulates and a range of oxidative pollutants that one would like to keep clear of. Keeping the airways clear is the job of the mucins – a family of large, heavily glycosylated proteins. Both secreted and tethered versions

## BOOK REVIEWS

of mucins abound and form a mat about 10  $\mu\text{m}$  thick, trapping and helping remove unwanted particles. They are major contributors to the viscoelastic properties of the mucus in airways, but also mediate cell–cell signalling, EGF receptor signalling and airway protection as presented in a series of four reviews in the section on respiratory physiology. Aberrant secretion and accumulation are associated with various lung diseases such as cystic fibrosis, asthma, chronic obstructive pulmonary disease, emphysema and lung cancers. The complex regulation of over 20 genes involved in mucin synthesis and secretion is starting to be revealed.

Aquaporins (AQPs), which serve to significantly enhance the permeability of membranes to water, are also associated with epithelia and their malfunction associated with a number of diseases. Rojek *et al.* review the mounting evidence that several aquaporins are not actually involved in water transport, but serve to mediate transport of small, uncharged solutes such as glycerol, urea and perhaps ammonia (but not ammonium ions). The rapidly expanding literature on aquaglyceroporins and unconventional AQPs is fraught with inconsistencies, including contradictory publications from the same group! The review is heavily biased to mammalian AQPs and restricted to the animal kingdom, leading one to wonder about the situation in plants which have to respond to huge changes in water and solute potentials. The regulation of AQPs is critical to drought response, and it is conceivable that aquaglyceroporins and unconventional AQPs play a comparable role in other responses.

Following Muybridge's work in the 1880s, studies of animal movement have relied on high-speed imaging and elaborate set-ups. Following the introduction of megapixel cameras with framing rates of 1–100 kHz, the study of musculo-skeletal function has expanded to the imaging of fluid flow around moving animals and appendages directly in digital format. This has greatly facilitated the calculation of forces in the surrounding fluids and a much more detailed understanding of the mechanics of animal locomotion. The examples presented in the review by Lauder and Madden are drawn from studies on fish, but similar work has been done on the flight of birds, bats and insects. Analysis of vortex wakes generated by swimming and flying animals have provided insight into the mecha-

nism of force generation and give the lie to the oft-quoted claim that 'aerodynamics shows that the bumble bee cannot fly'.

Static imaging also provides spectacular images that illuminate our understanding of the structure of biological objects. The use of X-rays for imaging is as old as X-rays. Westneat, Socha and Lee review the use of synchrotron radiation for X-ray imaging, using phase contrast and tomography to obtain nanometre resolution at a timescale that allows the monitoring of physiological processes. Non-destructive access to the innards of living, behaving insects have allowed the investigation of breathing, grasping and chewing, overturning conventional wisdom in the process. As John Lighton writes in *Current Biology* (2007) 'to see a familiar ant (*Camponotus vicinus*) turned into glass on the video monitor. I could not believe what I saw. That dark opacity I had known for decades, and which always seemed such a guardian of secrets, became a crystal paperweight alive with troubling mystery. It pulsed and wove its threads and beads while I watched lost in the wonder of seeing what few had seen before. Much I could interpret; much more I could not fathom. *This is what it was like to own a telescope during Galileo's time, I thought, but with the vision turned inwards not outwards*'. For instance, it was presumed that gas exchange in small insects like flies was purely diffusive. However, imaging studies revealed cycles of tracheal compression, while monitoring of gas composition showed active expulsion of  $\text{CO}_2$  even in flies. In larger insects, convection overcomes diffusive limitations in  $\text{O}_2$  delivery. Scaling studies indicate that the space available for trachea to pass through constrictions such as leg joints may impose upper limits on the sizes of insects. Indeed an analysis carried out after this review was written spans several different lineages and confirms this supposition. More, it suggests that in the Carboniferous, when  $\text{O}_2$  concentrations reached 35%, size limitations were less severe, consistent with the observation of giant insects. The largest such insects found are at the upper limit predicted at 35%  $\text{O}_2$  in the scaling exercise described.

These reviews serve to point out that even the staidest of fields can spring surprises – who would have thought ten years ago that X-rays would reveal the inner workings of insects? At the same

time, 'striving to bring molecular and mechanistic insights to problems concerning the physiology of the whole organism', emphasizes the central role that some of the usual suspects play. While calcium is not the answer to the question 'What is the meaning of life, the universe and everything?' (that would be potassium channels), this volume echoes Heilbrunn's proclamation in the 1940s 'Kalzium macht alles!' (calcium does it all).

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**Arthropod Borne Viral Infections: Current Status and Research, The Eighth Sir Dorabji Tata Symposium.** D. Raghunath and C. Durga Rao (eds). Tata McGraw-Hill Publishing Company Limited, 7 West Patel Nagar, New Delhi 110 008. 2008. 430 pp. Price not mentioned.

Austin Kerr, the founder-Director of Virus Research Centre, Poona (now, National Institute of Virology; NIV), while initiating the Centre wrote that research on arboviruses (arthropod-borne viruses) is like worshipping the Goddess Saraswati with four arms. According to him the arms represent the study of the virus itself; effects of the virus on its vertebrate host; study of the vector of the virus and study of the ecology of the vector, host and the virus. Now more than half century later, the study of arboviruses can be stated as: (a) the study of the genome of the virus and its gene sequence data; (b) the study of immunology, pathology and molecular events in the vertebrate hosts; (c) multiplication