Bioelectrochemistry: Principles and Practice. Volume 4: Bioenergetics. P. Graber and G. Milazzo, eds. Birkhauser Verlag, AG, Postfach 133, CH4010, Basel. 1997. 539 pp. Price: DM298.

Bioenergetics has always been a fascinating field, for its diverse views, for its extraordinary insights in the past, for the debates and for its pretensions to being more physical in its outlook than any other major field in biology. By being physical, one does not refer to merely the computational (cranking) approaches. It lies in its being close to that branch of physics that always played the Occam's razor, viz. thermodynamics. This volume no. 4 (wrongly referred to as no. 5 in the very introduction) in an informative collection of articles.

The volume starts with an overview, essentially pedagogic, by Dieter Walz, on nonequilibrium thermodynamics as applied to energy conversion, attractive to a teacher like me looking for good and readable material. Fortunately, I could not detect references to vectorial cross coefficients. Melandri's article on vectorial transport in fact deals with the inhomogeneity of the terrain caused by structurally asymmetric enzymes with due emphasis. However, little reference appears to be made with regard to the observed charge anisotropy across membranes for most membrane proteins. Westerhoff deals with global bioenergetics outlining the magnitudes of fluxes in the overall cycles of carbon, food chains even touching on evolution. The volume goes on to consider more specialized topics of energetics of anaerobic and aerobic bacteria before going on to an exhaustive account of the chloroplast and the mitochondrion. Cyanobacterial and algal photosystems I and II have all been discussed as also the cytochromes in some detail. Cytochrome oxidase falls short in view of its more recent structure elucidation.

There is a strange dichotomy emerging over the years in bioenergetics that this books fully bears witness to. Thermodynamics is opaque to mechanism. Yet we find increasing preoccupation with molecular mechanisms that find themselves oddly at variance with the espoused theories. Take the instance of the helicobacter. It was not an issue in this particular book since it was published recently. *Nature*, in a recent issue, proclaims the achievement stating that the positive charges inside the bacterium make it escape from the odds of survival against an acidic environment that this acidophile lives in. Contrast it with the chemiosmotic hypothesis. If bulk phase protons are to be involved, or any protons for that matter wherever we try to bury them, the influence of acidity and buffers would essentially reduce the energetic competence of protons. It is all right to generalize the notion of coupling. And yet, action of any uncoupler in inhibiting a dissipator without inhibiting the generator, a fundamental old-fashioned definition, is as often violated and we lose sight of simple chemistry. So we forget that CCCP or DNP are also ions and EDTA can act as an anion besides its ability to chelate Mg^{2+}. Paul Feyarabund, in a letter to me many years ago, observed that physical laws were bestowed on mankind from the brow of Zeus. There is no explicit reason why one should have one effect: one cause relationship other than the Platonic injunction. On the other hand, both of us agreed that Aristotelian notion of multiple causality has much meaning in understanding the real world. After all Aristotle said that there should be at least four causes, the first cause, the final cause, the material cause and the efficient cause. The heart of thermodynamics has also been in that it has been possible to define the energetic state of a system as a characteristic,

$$\varphi = u + pv - ts + \xi\omega,$$

such that $\xi\omega$ embodies a variety of energetically-competent intensive factors and their conjugate extensive variables. The first purpose of thermodynamics would be to identify possible causal factors (emphasis being on plural) to permit and facilitate enquiry and not to abridge it to a bare minimum of even a singular possibility merely because it is considered elegant. Feyaraband also reminds us of the view of Niels Bohr that elegance is strictly sartorial (i.e. for tailors). The identification of existence of cross coefficients should precede their quantitative contribution and espousal of any theory. This traditional wisdom, however, is overshadowed by emphasis on molecular explanations. At places in the text, various authors do mention reservations about the completeness of molecular explanations but this caution loses its punch when diluted into a surfeit of molecular explanations. This is the inherent schizoid tendency of the current-day bioenergeticist. If protons are involved, so be it, let us not worry about whether they are scalar or vectorial, ionic strength-dependent or not or even if they are energetically competent or not in so far they are there. In that sense the book is faithful to the mood.

An year at Rio, the beaches taught me the essence of modern bioenergetics that this book effectively summarizes. It relates to the use of the bikini: what it reveals is interesting... but what it conceals is vital.

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The special topic for this year's annual review of physiology is mechanosensitivity and if you are new to the subject and require an overview of what it is all about, it will be profitable to start from the last chapter of the book wherein a concise description of the various techniques employed to delineate the receptors, map the network of neurons involved, induce mutations and identify the role of various proteins in the process of transduction of mechanical stimuli in the nematode *C. elegans*, is elegantly presented. Conversion of mechanical stimuli into electrical impulses requires changes in the conduction of ions through channels. Interestingly such mechanosensitive channels of large conductance (MscL) have been identified and extracted from the cell membranes of *E. coli*. Stretch force transmitted to the channel through the lipid bilayer after incorporation of the channel in liposones was found to alter the conductance. Deletion or substitution of several residues affect channel kinetics or its mechanosensitivity. In a preceding chapter, the need to exercise caution while performing patchclamp experiments was sounded, since suction or pressure protocols involved in these techniques are known to induce morphological alterations. Plasma membrane, for example, may be decoupled from the underlying cytoskeleton, leading to hypo- or hyper-mechanosensitivity. How do cells themselves behave when subjected to mechanical stress? Ingber argues that all living cells have an internal prestress (pre-equilibrated stress) like the stress of a tensed bow or catapult. He advocates a 'tensegrity' (tensional integrity) model of cell. The intracellular cytoskeleton interconnects with the underlying extracellular matrix and the neighbouring cells through focal adhesion complexes at the cell base and by specialized junctional complexes at the lateral cell borders. Specialized proteins called integrins, cadherins and selections are involved in these contacts.

The recurring theme in many chapters spanning various systems of physiology seems to be channel activity, indicating that the study of these channels has moved to the forefront of research. A case for the involvement of potassium channels in detection of oxygen lack has been made out. Excised patches from glomus cells of the carotid body seem to respond to oxygen lack by closure of the potassium channels leading to depolarization. Such depolarization is known to alter the intracellular calcium concentration, leading to a change in the excitability of the cell. While this may not be the only mechanism responsible for sensing oxygen lack, it certainly merits further study as it raises the interesting possibility of alteration of channel protein structure on interaction with oxygen. Channels whose conductance changes with voltage are known as rectifier channels. Among these, the channels that allow inward flow of potassium ions are known as inwardly-rectifying potassium channels (Kir). Since the flow was against gradient, the rectification was called anomalous. Such channels play an important role in the maintenance of resting potential in the cardiac muscle. Genes encoding these channels have been identified and cloned. High level expression of these channels in *Xenopus* oocytes has led to detailed studies on the mechanism of voltage dependency of channel activity. Closure of these channels at positive potentials results from the blockage of the channel by magnesium ions or spermine, a polyamine. Chelation of polyamines by ATP or by inhibition of the key enzyme S-adenosyl methionine decarboxylase interferes with Kir channel function. A variety of stimuli – stretch, ATP, pH, voltage, cGMP, nitric oxide and protein kinases – seem to be involved in the regulation of potassium channels in the renal tubules. Arachidonic acid through an unidentified metabolite is involved in regulation of potassium channels in the thick ascending limb of renal tubules. A high potassium intake modifies the apical membrane potassium channel activity in the cells of collecting ducts, possibly through the secretion of aldosterone. ATP inside the cell can also affect either the channels or ion transporters through activation of lipid and protein kinases, alteration of cytoskeleton, modulation of binding proteins or chelation of polyvalent cations.

Chapters on gastrointestinal physiology mainly deal with endocrine aspects. Absorbing details on post-translational processing of gastrin or its intermediates, their physiological roles including trophic effects, have been described in the chapter on G-cell (gastrin-secreting cell). Infection by *H. pylori* through the release of ammonia might lead to degranulation of G-cells, hypersecretion of acid and formation of peptic ulcer. This is of relevance to us since a high percentage of Indians harbour this organism in their stomachs. Apart from the G-cell, the stomach contains another endocrine cell known as the enterochromaffin like cell (ECL) which releases histamine, the prime stimulus of parietal cells of the stomach. The interactions between various cells of the gastric mucosa have been dealt with in detail. Cells that secrete cholecystokinin (CCK) are situated in the intestine and in the brain, thus endowing this molecule with the dual function of hormone and neuropeptide. Recent findings on dietary and neuro-endocrine regulation of CCK cells and the second messengers involved have been explained. Special mention of the new proteins that act as releasing factors for CCK and are involved in mediation of feedback signals, has been made. In the chapter dealing with enteroglucagon, actions of the peptides derived from the parent molecule proglucagon have been described, most notable among them being glucagon-like peptide (GLP-1) which may be responsible for the ileal brake effect – inhibition of intestinal motility by the presence of unabsorbed nutrients in the ileum.

Angiotensin the octapeptide, acts through two types of receptors, AT1 and AT2. But the role of the latter is yet to be defined. The AT1 receptor mediates various responses like hypertophy, hyperplasia, hormone synthesis and ion transport in the heart, kidney and adrenal. It may also be involved in organ remodelling. This theme is further elaborated in the chapter dealing with the response of cardiomyocytes to mechanical stress. Stretch of these cells in the neonate stimulates a rapid secretion of angiotensin which induces cardiac hypertrophy. Two chapters are devoted to explain the role of endothelium in regulating the contractility of the heart and the tone of blood vessels. Endothelin produced by the endothelial cells in the heart increases isometric force while decreasing the actomyosin ATPase activity, thus promoting the efficiency of contraction. Endothelial cells are involved in mechanotransduction of shear stresses on blood vessels through modulation of several factors.

Rapid actions of steroid hormones which do not require genetic mechanisms, form the subject matter of one of the chapters on endocrinology. These include the action of aldosterone on lymphocytes, vitamin D3 on epithelial cells, progesterone on human sperm and of estrogens on blood vessels. These effects involve activation of phospholipase C, protein and tyrosine kinases, changes in pH and calcium. Mechanisms regulating apoptosis of ovarian follicles are detailed in another chapter. Gonadotropins, estrogens, cytokines and growth factors protect, while TNF-alpha and Fas ligand promote apoptosis.

Biochemists might find the chapters dealing with urea synthesis and cathepsin biology useful. Activity of ornithine–urea cycle enzymes is found to be higher in aquarians belonging to the family Betrachoididae, indicating their capacity to synthesize urea. Interesting details of rapid switch-over from ammonia excretion to urea synthesis during periods of stress in Gulf toad-fish have also been given. Cysteine proteases, although thought to be lysosomal mediators of protein degradation, play a role in apoptosis, pro-hormone processing and extracellular matrix modelling. The chapters on respiration seem to deal with structural aspects related to pulmonary vascular remodelling during normal development and in the pathogenesis of pulmonary hypertension. The role of lipofibroblasts found in the interstitium of the lung, in the development of alveoli and in pulmonary metabolism has been discussed.

To me the most remarkable chapter appears to be the preface by Clements chronicling the discovery, characterization and present understanding regarding the role of surfactant. Equally exciting is his family history and his description of his mother. He says 'With a mother like that around you don't need a father'. If you are eager to find out her qualities; well! begin at the beginning.

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