Appendix A2

Preface to the proceedings of the ICTP conference **"Nonlinear cooperative phenomena in biological systems"** held at Trieste, Miramare, 19-22 August 1977.

Research in nonlinear, cooperative phenomena in biological systems has mainly been concentrated on a few subjects such as neural networks and different subcellular phenomena, e.g. protein folding and solitary waves, each of which have become fields of their own, but to less extent on dynamics at the level of a single cell for which many vital functions are at work in the start and during the cell cycle. Needless to say, the living cell consists of condensed matter, and without correlations on membranes, protein and DNA-backboones, the cell could not function such as in differentiation and division. No signals would be transduced and there would be no life. Much of this normal "wild type" behaviour of a cell, living today, could often be better understood through studies of mutants and transformed cell lines, and through knowledge of the principles for selection and evolution.
Cellular dynamics and molecular assembly into biological systems are problems with a vast interface to physics. However, several important differences with respect to inanimate matter must be underlined. A biological system is usually more complex with large variations in order parameters and coefficients that control the interpolation between harmonic and displacive interaction modes. Moreover, this is not due to temperature variations. In contrast to inanimate matter systems, mostly driven thermally, living systems are chemically open and usually regulated lyotropically by various reactant concentrations, at chemically non-stationary conditions and at rather constant temperatures.
Thus many biological substances can form liquid crystalline structures in an aqueous environment, for instance cell membranes, provided that the concentration of the substrate reaches a saturation point at given temperature. Although temperature is still an important variable in determining the phase present, the concentration of one component with respect to the others is far more important. Hence, the behaviour of such a system is more lyotropic than thermotropic. This is even more pronounced for the various humoral factors reacting at the surface membrane, such as antigens, hormones and their receptors, the interaction of which regulates and drives the entire cell cycle dynamics in a quantal all-or-none fashion.
Studies in cellular metabolism thus take a new direction. From an initial stage of pathway identification, followed by a period of studies of pathway regulation through cooperativity, phosphorylation, feedback, feedforward and allostery, experiments now indicate that we have come to an era of pathway quantification. For instance, one single molecule can make the whole difference between cell division and premature abortion. This is fortunate because, if this was not the case the high fidelity in DNA replication would probably not be guaranteed and we would not exist. Thus the cell coherently counts the number of signals received, a behaviour that also indicates a more robust, solid like structure near the quantal threshold at high concentrations of recatants, after a rather liquid, displacive dynamics at low concentrations that permits the reactants to diffuse about in order to strategically meet. What we call "life" could then eventually be observed as fluctuations on the edge between order and chaos.
This awakes an old dream of a non-equilibrium statistical physics for biology, at the same time as it reveals the problems of stationary and thermotropic type theories when applied to non-equilibrium phenomena, and chemically open, lyotropically regulated systems. For instance, internalization of activated receptors takes place long before a stationary state is developed. This excludes the use of Hill, Langmuir and Michaelis-Menthen equations in this context, and of chemically stationary Ising and lattice type models, which reduce to the ordinary Langmuir response in the limit of vanishing cooperativity. The problems with such

models could also be identified through a wrong scaling behaviour and a threshold for response up to three orders of magnitude different from the assessed one.

The perplexing discovery that a dividing cell counts the number of signals received, which indicates an almost perfect coherence, might eventually also provide evidence for organized nonlinear excitations in biological systems. However, much to my regret, there was not sufficient time for a discussion of non-equilibrium statistical physics in chemically open and lyotropic systems. Therefore, also the question of driving mechanism for living systems came a little aside. A short summary of that part, compiled by Dieterich Stauffer, is published in this volume, which also includes a number of abstracts.

The aim of the meeting was to bring together researchers from different fields and to somewhat bridge the gap between experiments and theory. Despite the fact that we did not fully managed, according to the response, the meeting was a success. The scientific committee of this conference entitled "Nonlinear cooperative phenomena in biological systems", included Giorgio Careri (University of Rome), Stuart Kauffman (Santa Fee Institute), and Leif Matsson (University fo Gothenburg and Chalmers). Discussions with Per Bak, Hans Frauenfelder, Stig Lundquist, and Dieterich Stauffer also contributed significantly to the qualities of the meeting.

The order of contents of this book follows that of the speakers. Thereafter follows two reports by contributors who unfortunately could not participate, one on neural networks by Gerard Toulouse and a second one on ligand gated ion channels in chemically open systems. This is followed by a section of abstracts, and a short summary of the panel discussion.

Finally I want to thank the International Centre for Theoretical Physics (ICTP), its director Miguel Virasoro, Yu Lu and Hilda Cerdeira for the opportunity of holding this conference at ICTP. I also thank the administrative staff, in particular Valery Shaw, for their kindness and efficiency in all the arrangements and hope that all participants enjoyed the meeting as I did myself. I also thank Reymond Emanuelsson for typing five of the contributed manuscripts in the correct formate.

At an early stage in the planning of the meeting Stig Lundquist suggested that it should be held at ICTP, and performed as an Adriatico Research Conference. As the leader of this series of conferences in condensed matter physics at ICTP, during three decades, parallel to his many activities at the University of Gothenburg and Chalmers, the Royal Swedish Academy of Sciences, the Nobel Committee for Physics and many other things, he has also stimulated this type of interdisciplinary activities. It is therefore a pleasure for me to dedicate this volume to Stig Lundquist.

Leif Matsson