

## **Introduction**

### **Symposium on Intercellular Communication Stuttgart, 1982**

D. F. Hülser

Abteilung Biophysik, Biologisches Institut, Universität Stuttgart,  
Ulmer Straße 227, D-7000 Stuttgart-60, Federal Republic of Germany

Intercellular communication is a postulate of complex multicellular organisation. Signal transfer between cells is possible in different ways: 1.) Long distances of up to 1 m may be bridged by molecules which are produced in distinct cells and are released into the extracellular fluid where they are distributed and interact with receptors on the surface of their target cells (e.g., humoral interaction). 2.) Transmitter substances which have a limited life span or which can be inactivated by inhibitor molecules spread signals only over shorter distances (e.g., synaptic cleft, ~200 nm). 3.) Information can also be exchanged by direct membrane contact when two molecules interact with each other directly or via linker molecules (e.g., immune system). 4.) Intercellular communication is also possible by channels between adjacent cells which permit the exchange of ions and molecules and the spread of electric currents; many of those pores are arranged in the membranes of the contacting cells as a quasicrystalline structure forming the gap junction.

A national symposium on "Intercellular Communication" in Stuttgart on 16 and 17 September 1982 serving the aim of increased "interlaboratory communication" covered most of the above aspects. It was sponsored by the Deutsche Gesellschaft für Biophysik and the Dr. Karl Thomae GmbH whose help is gratefully acknowledged. The following papers were all submitted at this meeting.

Most of the contributions dealt with intercellular communication mediated via gap junctions. Electronmicroscopic investigations of these structures are presented by Hülser and Brümmer where also physical data of the gap junction pores are listed. A multicellular organisation like a two-dimensionally growing cell culture is already a rather complex system which develops subpopulations and shows a cell density dependent inhibition of growth (Adam et al.). Apparently a two-dimensional system is unable to regulate its intercellular molecule exchange by closing its gap junctions. In a monolayer channels remain in the open position regardless of the inhibition of proliferation. However, an endogenously regulated continuous closing of gap junctions occurs as soon as cells are allowed to grow to three-dimensional multicell spheroids (Hülser and

Brümmer). This age dependent decoupling of cells in a spheroid is accompanied by a reduction of the adenylate cyclase activity (Dertinger et al.). The importance of threedimensional growth for intercellular regulations via gap junctions is underlined by Rink. He reports that the main intrinsic polypeptide of lens junctions is synthesized only when the cultured lens cells formed three-dimensional aggregates.

Therefore, in-vivo experiments are necessary to clarify the mechanism of gap junction controlled regulation processes. In-vivo experiments provide a sufficient yield of purified gap junction proteins for the production of gap junction antisera, which led to the investigations of the specificity of gap junction proteins and their synthesis- and degradation-pathways (Willecke et al.). Gap junctions are not only found in non-exitable cell systems, they are also present in neuronal systems, as "electric synapses". In the earthworm (Berger) two kinds of gap junctions connect the axon segments in the medium giant axon either directly or via accompanying cells. Electronmicroscopic studies on skeletal muscle exhibited an acetylcholinesterase production in the muscle fiber of adult mice (Dauber). Whether these molecules are also distributed via gap junctions is still an open question. In the control of lymphoid cell proliferation each of the four above mentioned intercellular signal transfer mechanisms might be involved. Peters and Müller-Hermes review this system and develop an unifying hypothesis.

The aggregation of single undifferentiated cells and their final formation of fruiting bodies with two types of differentiated cells can be observed under controlled in-vitro conditions for the slime mold *Dictyostelium discoideum*. Gap junctions between these cells have not yet been demonstrated. In his presentation, Gerisch provided evidence that only defined periodic pulses of cAMP led to an aggregation of single cells, and that the movement of the cells is regulated by a phosphorylation of myosin (no paper in the following series). The endogenous propagation of cAMP pulses is accompanied by  $\text{Ca}^{2+}$  uptake, as Malchow has demonstrated with  $\text{Ca}^{2+}$ sensitive electrodes. This uptake is dependent on the differentiation status of the cells. A particular periodicity of the cAMP pulses is critical for the cells' ability to resolve them as discrete signals (Wurster). A 2-min rhythm does not lead to a differentiation of the cells but is still resolved as a discrete signal at the level of cGMP which is part of the pathway that regulates developmental processes in this slime mold.