## = INTRODUCTION =

## The Conference "Microbial Communication"

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The present special issue of the journal Microbiology contains papers by the authors that presented reports at the conference "Microbial Communication," held at the Bakh Institute of Biochemistry, Russian Academy of Sciences, on November 11, 2005. On the whole, these papers cover almost the whole range of problems of microbial intercellular communication, including microorganism-plant symbiotic interactions. It is clear that the limited volume of a journal paper does not allow a complete review of the present state of the art in a given field. The aim of this issue is, firstly, to provide a survey of concepts and approaches that have been developed in Russia and, secondly, to acquaint the reader with the laboratories and researchers engaged in work on microbial communication. The organization of this conference was inspired by the following motifs.

For a long time, the capacity of individual cells in a growing microbial population for growth, division, and flexible switching of metabolic flows, as well as the absence of pronounced specialization of individual cells within a population, provoked the widespread view that a bacterial cell is a solitary organism whose behavior is little dependent on the other cells of the population. However, the self-sufficiency of a bacterial cell turned out to be rather limited. The revision and generalization of a great body of information on the biology of prokaryotic and eukaryotic microorganisms allowed a concept to be put forward that considers a microbial population (a culture, colony, biofilm, etc.) as a multicellular organism with a complicated system of intercellular interactions [1]. This, in turn, generated interest in the "languages" which the cells (belonging to the same or different species) use to communicate with each other.

Chemical communication is the best-studied mechanism of information transfer between cells in growing microbial populations; it is provided for by the synthesis of metabolites with specific signaling functions. Although the regulatory effect of extracellular metabolites on the growth of microbial cultures was revealed as early as in 1904 by Rahn (cited in [2]), intensive studies of the functional role of communicatory molecules secreted by the cells into the medium were started only in the 1970s.

The so-called A factors, secreted by several streptomycetes, were discovered by A.S. Khokhlov and identified as derivatives of  $\gamma$ -butyryl lactones. This pioneering finding generated great interest of both fundamental scientists and biotechnologists in the investigation of microbial autoregulators. By using a test system involving mutants or dissociants of *Streptomyces griseus* with impaired cytodifferentiation (formation of aerial mycelium) and synthesis of secondary metabolites (streptomycin production), it was shown that these impairments were caused by the absence of the A factor; its addition together with inoculum restored the impaired properties of the culture.

At present, along with hundreds of original publications concerning the role of extracellular autoregulators (microbial metabolites that fulfill signaling functions in the population), several reviews are available [3-6]. Much attention has been given to autoinhibitors of microbial adaptation, defined in [7] as metabolites that restrict the population size within the limits dictated by environment, and to pheromones, which are metabolites that regulate the reproductive function and the structure of the population. The best studied communication system is the so-called "quorum sensing," involving extracellular signaling metabolites. When the cells of a producer reach a critical concentration (quorum) in the medium, these metabolites cause autoinduction of their own synthesis and the expression of a number of genes of the stationary growth phase. The estimation of the critical cell number involves the action of various low-molecular-weight compounds, such as amino acid derivatives, peptides, etc. Bacterial pheromones regulate such important events in the prokaryote life-cycle as sporulation, the formation of resting forms, and the reversion of cells to the active state.

Another type of intercellular communications is responsible for changes in the kinesthetic behavior of the cells and physical contacts between cells (cell aggregation) and between cells and solid surfaces (cell adhesion); it plays a key role in the formation of biofilms and bacterial mats and in cell proliferation under unfavorable environmental conditions.

Intercellular communication is of special importance for symbiotic interrelations between microorganisms and host plants. In the last decade, it was revealed that bacteria successfully use the biologically active compounds of the host macroorganism in their regulatory processes. Thus, pathogenic bacteria are able to use human cytokines for resuscitation of resting forms and stimulation of the growth of vegetative cells; symbiotic azospirilla are competent with respect to lectin of their host plant, which, like human cytokines, fulfills quite a different primary function in the host organism.

Russian researchers have been at the forefront of the development of several lines of research in the field of microbial communication; therefore, many of them have had to overcome difficulties inevitable for those who strive to gain insight into new problems.

The conference "Microbial Communication" aimed to provide its participants with the opportunity to present their own experimental data and to discuss them in the context of data obtained by other research teams. It is hoped that the exchange of information between participants will promote progress in investigations of microbial communication. The conference was organized by the Bakh Institute of Biochemistry, Russian Academy of Sciences (INBI RAS), Moscow, and the Institute of Biochemistry and Physiology of Plants and Microorganisms, Russian Academy of Sciences (IBPPM RAS), Saratov, with the active assistance of the Society of Biochemists and Molecular Biologists and the Microbiological Society; it was held at the INBI RAS.

The conference was attended by 112 participants, who came from Moscow, St. Petersburg, Kazan, Saratov, Perm, Ufa, Orenburg, Irkutsk, Krasnoyarsk, Ivanovo, and from two scientific centers situated near Moscow, Pushchino and Obolensk. Participants from leading research institutes and institutes of higher education, including those affiliated with the Russian Academy of Sciences, Russian Academy of Agricultural Sciences, and Russian Academy of Medical Sciences, delivered 16 oral reports and 8 poster presentations.

The reports included experimental data on the communication and signal exchange between bacteria, their social behavior, and intercellular communication during the formation of colonies and biofilms. Most of the oral reports and poster presentations were devoted to the functional role of extracellular autoregulators and molecular mechanisms of cell adaptation to stress factors and to the formation of resting forms of bacteria and their reversion to vegetative growth.

The conference was opened by A.V. Oleskin (Biological Faculty, Moscow State University), who highlighted modern concepts of a microbial population as a single whole, emphasized the contribution of Russian scientists to the advances in this field, and reported his own experimental data on the regulatory functions of hormones of higher plants (serotonin and others) in the development of microbial cultures.

Five reports in the first section were devoted to the cell-density-dependent behavior of bacteria (the "quorum sensing" system). At present, it is universally recognized and supported by the great bulk of experimental data that bacteria are capable of monitoring the cell number in their population and of determining their strategy of survival in dependence on population density. I.A. Khmel (Institute of Molecular Genetics, Russian Academy of Sciences) presented an overview of the problem, and four reports were devoted to specific aspects of the research into the quorum sensing phenomenon (see papers by V.V. Aleshin, E.V. Babynin, G.B. Zavil'gel'skii, I.A. Khmel and their coauthors in this issue).

Extended discussions were also devoted to other strategies of microbial survival in natural ecosystems and to the role of intercellular communication in the realization of these strategies. These problems were examined in the reports that considered the regulation of biofilm formation (Yu.M. Romanova, Gamaleya Research Institute of Epidemiology and Microbiology, Russian Academy of Medical Sciences), the role of the intercellular matrix in bacterial communication (I.V. Botvinko, Biological Faculty of the Moscow State University), the formation of L-forms of pathogenic bacteria and their possible reversion to the initial state with pathogenic properties retained (I.B. Pavlova, All-Russia Research Institute of Veterinary Sanitation, Hygiene, and Ecology, Russian Academy of Agricultural Sciences).

A number of reports were devoted to the study of low-molecular-weight extracellular autoregulators of bacteria, which provide intercellular communication to ensure cell survival under various stresses, both those envisaged in the ontogeny of microbial cultures and those induced by various adverse factors. Considerable interest was aroused by the studies of G.I. El'-Registan, A.L. Mulyukin, and Yu.A. Nikolaev (Winogradsky Institute of Microbiology, Russian Academy of Sciences), the reports by T.Ya. Vakhitov (Research Institute of Highly Pure Preparations) and A.B. Margulis (Kazan State University), and the communication by V.P. Korobov (Institute of Ecology and Genetics, Russian Academy of Sciences) about the factors of chemical communication involved in the control of the development of gram-positive bacteria.

In recent years, resting (dormant) forms of bacteria and the regulation of their resuscitation have become a subject of great interest for biologists of different profiles, practical bacteriologists, and biotechnologists. This important problem was considered in the reports by A.S. Kaprelyants (INBI RAS), A.L. Mulyukin (Winogradsky Institute of Microbiology, Russian Academy of Sciences), and S.A. Voloshin (INBI RAS).

The final section was devoted to the role of extracellular microbial metabolites in the interactions between microorganisms and plants. The data obtained in experiments with azospirilla (L.P. Antonyuk, Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences) and cyanobacteria (O.A. Gorelova, Biological Faculty of Moscow State University) were reported. Since not all of the participants could present their data as oral reports at the one-day conference, some of the communications were presented as posters, in particular, the studies of O.V. Rybal'chenko, M.N. Rudchenko, E.L. Sumina and their coauthors (see corresponding papers in this issue).

The conference was concluded by a discussion of the presented reports and of the present-day state and prospects of development of this field of microbiology in our country. The conference demonstrated that many research groups in Russia are engaged in solving the problem of chemical communication in microbial populations by using up-to-date approaches. In spite of the extremely tough financial conditions that have persisted over almost two decades, these groups retain their high scientific potential; on the basis of the knowledge that they have obtained on autoregulation of microbial populations, they have put forward original scientific approaches for solving this fundamental problem.

Obviously, the time allotted for the conference was insufficient for extensive discussion of all of the considered problems. Many participants recommended organizing a three- or four-day conference. This can be realized within the framework of the conference on microorganism-plant interactions that is planned to be held in 2007 at IBPPM RAS in Saratov. The reports presented at the present conference argue for this suggestion. Thus, mechanisms responsible for the regulation of bacterial population density are of great importance for understanding such events as the colonization of plants by microorganisms, the formation and viability of biofilms, the formation of resting forms and their reversion to the active state, stress responses of microorganisms, and the ways of utilization of biologically active substances of the host macroorganism by microbes. All these aspects of microbial communication are of vital importance for the development of microbiology, microbial ecology, molecular genetics, and biochemistry of microorganisms, and for gaining insight into the problem of plant-microorganism symbiosis.

It is clear that the progress in the studies of microbial communication depends essentially on financial support. At present, there is no doubt as to the importance of this problem for the development of medicine, preservation of the environment, and progress in several lines of biotechnology, including agricultural biotechnology. This gives grounds to anticipate financial support from Russian sources, as well as development of cooperation with foreign partners.

On behalf of the researchers engaged in the problem of microbial communication, we thank the directors of the Bakh Institute of Biochemistry, Russian Academy of Sciences, for their help in the organization of this conference and the editorial staff of the journal *Microbiology* for the publication of a special issue devoted to this important field of modern microbiology.

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