Multicellular Organization in Microbes (Coordination in Microbes)

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Introduction

- In year 1988, *Scientific American* published an article entitled “Bacteria as Multicellular Organisms”. It was based largely on the observation of pattern and organized cellular differentiation in the colonies of many bacterial species, including *E. coli*.
- Multicellularity was still widely considered a specialized adaptive strategy of particular groups, such as the *Myxobacteria* or *Actinomycetes*.
- Intercellular communication and concerted multicellular activities are now generally accepted to be common among bacteria.
- The change in thinking is due mainly to the discovery that “quorum-sensing” signal molecules, in particular the *N*-acyl homoserine lactones (AHLs) in Gram-negative species, are used throughout the eubacterial kingdom to regulate the expression of a wide variety of phenotypes.
- The past decade has also witnessed the discovery of new phenomena, such as autoaggregation of chemotactic bacteria and coordinated behaviors in complex colony morphogenesis.
- The molecular basis of intercellular coordination is being clarified in multicellular taxa such as the *Myxobacteria* and *Streptomycetes.*

Core Concepts of Bacterial Multicellularity

Briefly stated, the core concepts of bacterial multicellularity may be summarized as follows:

1. Bacterial cells have communication and decision-making capabilities that enable them to coordinate growth, movement, and biochemical activities.
2. Examples of communication and coordinated behaviors are widespread (possibly ubiquitous) among bacterial taxa and are not limited to a few groups with a specialized multicellular vocation.
3. Bacterial populations derive adaptive benefits from multicellular cooperation and their ability to integrate the diverse activities of different cells. These benefits include (but are not limited to):

   (*a*) More efficient proliferation resulting from a cellular division of labor;

   (*b*) Access to resources and niches that cannot be utilized by isolated cells;

   (*c*) Collective defense against antagonists that eliminate isolated cells; and

   (*d*) Optimization of population survival by differentiation into distinct cell types.

Intercellular Communication

- Gram-positive and Gram-negative bacteria use quorum sensing communication circuits to regulate a diverse array of physiological activities.
- Quorum sensing is the regulation of gene expression in response to fluctuations in cell-population density.
- Quorum sensing bacteria produce and release chemical signal molecules called autoinducers that increase in concentration as a function of cell density.
- The detection of a minimal threshold stimulatory concentration of an autoinducer leads to an alteration in gene expression.
- These processes include symbiosis, virulence, competence, conjugation, antibiotic production, motility, sporulation, fruiting body formation and biofilm formation.
- In general, Gram-negative bacteria use acylated homoserine lactones as autoinducers, and Gram-positive bacteria use processed oligo-peptides to communicate.
- Recent advances in the field indicate that cell-cell communication via autoinducers occurs both within and between bacterial species.
- It is to be expected that intracellular systems responding to intercellular signals will be molecular computing networks allowing each cell to make appropriate decisions and adjust its activity to coordinate with other cells in the group.
- This expectation is very much in line with current thinking about the decision making capabilities of cells in higher organisms.

Coordinated Multicellular Behaviors

Colony Development

- Many microbiologists no longer remember that most bacteria proliferate and survive attached to surfaces.
- When we examine surface cultures, we find that bacteria differentiate biochemically and morphologically, and they interact in ways that produce spatially organized populations.
- It is worth pointing out that colony development and collective motility phenomena in bacteria hold valuable lessons for understanding the formation and development of biofilms, perhaps the most widespread multicellular prokaryotic structures in nature.

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Swarming

- Observed in both Gram-positive and Gram-negative species. Swarming involves rapid migration over a surface by groups of elongated, hyperflagellated “swarmer” cells encased in exopolymers.
- Length and hyperflagellation distinguish swarmer cells from “swimmer” cells, which resemble motile *E. coli* and are capable only of swimming in fluid, not of migrating over agar surfaces.
- Swarming has been studied most intensively in *Proteus mirabilis* and *Proteus vulgaris*.
- This multicellular behavior has been mostly observed in controlled laboratory conditions and relies on two critical elements:

  1) the nutrient composition and 2) viscosity of culture medium (i.e. % agar).
- In some species, swarming motility requires the self-production of biosurfactant to occur.
- Biosurfactant synthesis is usually under the control of an intercellular communication system called quorum sensing.
- Biosurfactant molecules are thought to act by lowering surface tension, thus permitting bacteria to move across a surface.
- Swarming bacteria undergo morphological differentiation that distinguish them from their planktonic state.
- Cells localized at migration front are typically hyperelongated, hyperflagellated and grouped in multicellular raft structures.
- The fundamental role of swarming motility remains unknown. However, it has been observed that active swarming bacteria of *Salmonella typhimurium* shows an elevated resistance to certain antibiotics compared to undifferentiated cells.

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More Efficient Proliferation from Cellular Division of Labor

- Nitrogen-fixing heterocyst formation in filamentous photosynthetic cyanobacteria was cited to illustrate how two cell types could cooperate in a monospecific multicellular population.
- Likewise, the ability of Proteus to spread rapidly over an agar surface depends on swarmer cell differentiation, and the velocity of spreading is directly related to the rate of biomass production.
- Monocultures also display larger-scale functional differentiation of various cell groups, such as the stalks and sporangia in Myxobacterial fruiting bodies and, Substrate and aerial mycelia in Streptomyces.

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Access to Resources and Niches

- In nature, many bacteria break down complex organic polymers, requiring the concerted action of many cells.
- The predatory *Mxyobacteria* utilize a "wolf pack" strategy to attack and lyse their prey organisms by liberating digestive extracellular enzymes and absorbing the cell contents.
- Using *M. xanthus* and casein as a model substrate, substrate utilization was found to be dependent on population density.
- Interestingly, groups of *M. xanthus* cells can migrate chemotactically but individual cells cannot.
- *M. xanthus* grazes on cyanobacteria in ponds.
- However, the aqueous environment can dilute both the lytic exoenzymes and liberated nutrients.
- Thus, the predators construct spherical colonies and trap prey organisms in pockets where lysis and feeding can occur efficiently, showing that multicellular behavior to permit resource utilization.

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Collective Defense Against Antagonists That Eliminate Isolated Cells

- Many agents can effectively kill isolated bacterial cells in suspension but are ineffective against dense or organized populations of the same bacteria.
- One example is catalase protection against oxidative damage.
- There is no difference in the survival to hydrogen peroxide challenge of *cat*$^{-}$ (catalase-defective) and *cat*$^{+}$ (catalase-positive) *E. coli* strains when tested in dilute suspension, but in thick suspensions or in microcolonies on an agar surface, the *cat*$^{+}$ strain shows much greater resistance.
- Penicillin-resistant biofilm composed of penicillin-sensitive *Staphylococcus aureus* bacteria.
- Many bacteria produce antibiotics, generally under the control of intercellular communication and quorum-sensing systems to eliminate competitors for nutrients and nich.

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Optimization of Population Survival by Differentiation into Distinct Cell Types

Sporulation and Formation of Dormant Cells

- The most obvious diversification is formation of spores or other resistant, dormant forms.
- Among nonsporulating bacteria, dormant forms can survive for long periods under difficult conditions.
- An interesting corollary to multicellular control of dormancy is the suggestion that exit from dormancy involves intercellular signaling and “wake-up” pheromones, both in isolated cells and in biofilm populations.
- This may explain why many dormant cells are difficult to culture from dilute suspension but not from denser inocula.
- An extracellular protein needed for resuscitation of dormant *Micrococcus luteus* cells has been reported.

Exchange Of Genetic Information

- Besides sporulation, *Bacillus subtilis* populations can develop subpopulations competent for DNA uptake with potential to incorporate new genetic information and thereby novel proliferation and survival abilities.
- Development of competence is a multicellular process involving intercellular signaling and elaborate signal processing.
- In *B. subtilis*, competent cells can take up DNA from any source.

Questions

- Write an essay on multicellular organization in bacteria.
- Explain significance of multicellular organization in bacteria.
- What is quorum sensing? How autoinducers important for intercellular communications.
- Write a short note on quorum sensing.