Social Behaviour in Bacteria

Dipankar Chatterji,
Molecular Biophysics Unit,
Indian Institute of Science, Bangalore
(dipankar@mbu.iisc.ernet.in)
Social

from Latin socialis -‘allied’,
from socius -‘friend’.
Social Animals

Images taken from google images
Social Insects

honeybee
(\textit{Apis mellifera})

worker

queen

drone

© 2006 Encyclopædia Britannica, Inc.
Social Humans
Bacteria

- Prokaryote
- Unicellular
- Good & Bad
- Division through binary fission

Scanning Electron Micrograph of *Escherichia coli*. Image taken from google images
Bacteria & Social?

What is the need for asexual unicellular organisms to display social behaviours
Bacteria are indeed social!

Herbert Spencer

- Contemporary of Darwin
- Known for ‘survival of fittest’
- Popularized ‘Altruism’
- First to apply term ‘altruism’ to single celled organism

(1820-1903)

Bacteria are indeed social!

Image taken from wikipedia.org
Peter Kropotkin

- Russian geographer, economist, activist, philologist, zoologist, evolutionary theorist, philosopher

- “...we must be prepared to learn some day, from the students of microscopical pondlife, facts of unconscious mutual support, even from the life of micro-organisms.” Kropotkin (1902)

(1842-1921)
Social behaviour of microorganisms was hardly explored

By the end of last century, the studies on the social behaviour of microorganisms bloomed
Social Behaviour

• A behaviour is social if it has consequences for both the actor and the recipient.

• Social behaviours can be categorized according to the fitness consequences they entail for the actor and recipient.
Classification of social behaviour

Foster KR, *Social behaviour: genes, ecology and evolution*
Secreted products used for social behaviour in bacteria

- Enzymes
- Extracellular substances
- Siderophores
- Autoinducers
Siderophores: Iron carriers

Selfishness or cheating

• Tragedy of commons
• *Pseudomonas aeruginosa* form biofilms in the lungs of cystic fibrosis patients and secrete siderophores (iron carriers vesicles) to maintain infection
• It is found that some cells do not secrete siderophores
• This reduces the overall virulence
• Hence, selfishness is bad in the long run

Foster KR, *Social behaviour: genes, ecology and evolution*
Tragedy of commons
Mutual benefit or Mutualism

• The host: the termite *Mastotermes darwiniensis*
• A symbiont *Mixotricha paradoxa* that helps to break down cellulose. The “fur” on the surface is actually the flagella of symbiotic spirochete bacteria that helps it to swim around

Altruism: *mazEF* toxin-antitoxin system of *Escherichia coli*

During normal growth, toxin bound to antitoxin

Phage infection causes destruction of less stable antitoxin leading to release of the toxin, which kills the infected cells and saves the uninfected population

Spread of antibiotic resistance

Sensitive population with very few resistant mutant → Enrichment of resistant mutants → Entire population becomes resistant
Antibiotic resistance is a phenotype acquired by bacteria during prolonged treatment due to selection pressure.

Attributed by several factors like mutations in the antibiotic binding site or due to other physiological changes.
Time line of antibiotic resistance

Antibiotic deployment

Antibiotic resistance observed

“A post-antibiotic era—in which common infections and minor injuries can kill—far from being an apocalyptic fantasy, is instead a very real possibility for the 21st Century.”

http://hub.jhu.edu/2014/07/24/antibiotics-in-animal-feed
http://switchboard.nrdc.org/blogs/akar/antibiotic_resistance_racing_t.html
• The process repeated ten times with increasing concentration of antibiotics.
• Most of the cells were antibiotic sensitive, only very few cells were antibiotic resistant.
• These highly resistant isolates produce the signalling molecule indole, which activates drug efflux pumps and other protective mechanisms in susceptible kin.
• This altruism allows weaker constituents to survive and to have the chance of beneficial mutation.

Spite

- Bacteriocins are antimicrobial toxins produced by bacteria that target closely related strains and species, and to which the strain is immune.

- *Photorhabdus asymbiotica* (asy) and *Xenorhabdus nematophilus* (X3) two are bacteriocin-producing, insect-killing bacteria and independently they elicit higher mortality in the host.

- When both the bacteria happen to infect the host caterpillar *Galleria mellonella*, the mortality of caterpillar is reduced

In-vivo and In-vitro proofs of spite

Cannibalism in Bacillus

Sporulation is an energy-intensive process that is irreversible after the early stages. If food resources become available during later stages, sporulating cells would be at a disadvantage relative to bacteria that could initiate growth immediately. For the bacterial population as a whole, it is beneficial to delay the onset of sporulation.

Rhizobiome: the microbes around the roots of the plant

• Studies have shown that there are up to 10 billion bacterial cells per gram of soil in and around plant roots, a region known as the rhizosphere.

• Dozens of species appear to suppress plant disease by excreting substances that ward off pathogenic microbes or occupying niches otherwise taken up by the pathogens.

• The rhizobiome depends heavily on the soil type.

Nitrogen Fixation by Legumes

The Littlest Farmhands

- Biological nitrogen fixation is the process that changes inert $N_2$ into biologically useful $NH_3$.
- This process is mediated in nature only by N-fixing rhizobia bacteria (*Rhizobiaceae, α-Proteobacteria*).
- In legumes and a few other plants, the bacteria live in small growths on the roots called nodules.
- Within these nodules, nitrogen fixation is done by the bacteria, and the $NH_3$ they produce is absorbed by the plant.
- Nitrogen fixation by legumes is a partnership between a bacterium and a plant.

Gut Microbiome

• It helps the body to digest certain foods that the stomach and small intestine have not been able to digest.
• It helps with the production of some vitamins (B and K).
• It helps us combat aggressions from other microorganisms, maintaining the wholeness of the intestinal mucosa.
• It plays an important role in the immune system, performing a barrier effect.
• A healthy and balanced gut microbiota is key to ensure proper digestive function.

http://www.gutmicrobiotawatch.org/en/gut-microbiota-info/
• **Competition for Resources**

• **Restaurant Hypothesis**

• Invading Pathogens must compete with resident microbiota to enter into a restaurant or they will be eliminated

• **Microbes (ASM) aug.2015**
Food for thought

No. of human cells: $10^{13}$
No. of bacteria on humans: $10^{14}$
No. of human genes: 30,000
No. of bacterial genes in human 30,000,000

Microbes also display an impressive ability to detect the density of their own and other species through “quorum sensing”.

- **Quorum**: A gathering of the minimal number of members of an organization to conduct business
- **Quorum Sensing**: sensing who is around
- It involves a wide variety of secreted compounds known as autoinducers, including some packaged in vesicles
- If cells secrete a chemical, then as cell density goes up, so will the local concentration of the chemical. By responding to the chemical, therefore, the cells can respond to their own density.

Biofilm formation is a developmental process in which bacteria undergo a regulated lifestyle switch from a nomadic unicellular state to a sedentary multicellular state.

Autoinducers: molecules used for intra- and interspecies communication

Acyl homoserine lactone autoinducers

Core molecule

Vibrio fischeri

Vibrio harveyi

R groups

Pseudomonas aeruginosa

Pseudomonas aeruginosa

Oligopeptide autoinducers

Staphylococcus aureus

Streptococcus pneumoniae

Biofilms: a city of microbes

• Biofilm is a structured community of bacteria embedded in self-produced polymeric matrix and attached to abiotic or living surface.

• Biofilms can be composed of multiple species or single.

• Biofilms protect bacteria from antibiotics and other environmental insults. They are cause of nosocomial infections as well as persistent infections.
R. Mathew, R. Mukherjee, R. Balachandar and D. Chatterji Microbiology; 152: 1741-1750.

*Mycobacterium smegmatis* Mc²155 biofilm grown at the air–water interface in a plastic Petri dish.
Altruism in bacteria

- Biofilms: City of microbes held together by a series of extracellular substances such as cellulose and adhesins
- For instance, dental biofilms
- They are everywhere
- Antibiotic treatment is not effective
- Some die for the good of others and the remaining one grows back

*Mycobacterium smegmatis* biofilm: Gupta and Chatterji (2015)
Biofilms

*Mycobacterium smegmatis* biofilm

Dental biofilm: a multispecies biofilm
Image taken from google images
D-amino acids trigger biofilm disassembly

- Compounds that could disrupt and disassemble biofilms can be used as therapeutics.
- Richard Losick’s group reported that a mixture of D-amino acids comprising D-leucine, D-methionine, D-tyrosine, and D-tryptophan that could act at nanomolar concentrations and trigger biofilm disassembly.
- Same group reported that D-amino acids indirectly inhibit biofilm formation in *Bacillus subtilis* by interfering with protein synthesis.

Cyclic-di-GMP

Formation of biofilm leads to the antibiotics tolerance because antibiotics fail to penetrate biofilm matrix to reach bacteria. It is often regulated by quorum sensing phenomenon (cell to cell communication).

(Høiby et al., 2010, IJAA)
Persistence in bacteria – A bet-hedging strategy

Biphasic killing of *M. tuberculosis* in mice by antibiotics

Stringent response - A social behavior in bacteria

Stress and starvation

GTP/GDP + ATP

(\textit{p})ppGpp

Rel

Biofilm formation

Normal cell

Growth arrest

Antibiotic tolerance

Persister cell

Toxin-antitoxin modules activation

Persistence

Stringent Response in Bacteria

**Nutrient starvation**
(Amino acid, Carbon, Fatty acid, Iron, Phosphorous)

**Environmental stress**
(UV, Salt, Acid, Alkali, Heat, Cold, Osmolar, Antibiotics)

---

**STRINGENT RESPONSE**

Reduction to a minimal unit

**Macromolecular Degradation**
- Fatty acid breakdown
- Proteolysis
- Amino acid biosynthesis

**Macromolecular Biosynthesis**
- tRNA and rRNA synthesis
- DNA replication
- Cell division
Key Players: Rel, (p)ppGpp & RNA polymerase

'Magic Spots'

MS-I : ppGpp

MS-II : pppGpp

Cashel and Gallant (1969)


Magnusson et al., (2005)
**Stringent Response in *Mycobacteria***

**Mycobacterium smegmatis mc²155**


---

**Rel**

**Rel** subunits of RelMsm (MSMEG_2965; 797 aa)

---

- **Catalytic domains**
- **Regulatory domains**

---

- **Reciprocal regulation of synthesis and hydrolysis activity**
  

- **Regulation of NTD catalytic activity by CTD in RelMsm**
  
Known nucleotide based second messengers in bacteria

- cAMP (1957)
- (p)ppGpp (1969)
- cGMP (1974)

Cyclic-di-guanosine monophosphate (c-di-GMP)


- cAMP
- (p)ppGpp (+12)
- cGMP (+5)
- c-di-GMP (+13)
- c-di-AMP (+21)
- c-AMP-GMP (+4)

Timeline:
- 1957
- 1969
- 1974
- 1987
- 2008
- 2012
Acknowledgement

Kuldeep Gupta

Anushya Petchiappan