CDS 270-2, Spring 2003

Cell-Cell Communications and Signal Decay During Antagonistic Microbial Interactions

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Project Background

Species are often in competition with each other for limited resources, *e.g.* food. This is as true for bacteria as it is for larger organisms. Many species of bacteria have evolved mechanisms to leverage their position within a community of diverse organisms. For example, a number of bacteria make antibiotics that inhibit the growth of, or actually kill other microbial species. Indeed, most antibiotics used clinically are derived directly from microbes grown industrially, or from secondary chemical transformations of these naturally occurring compounds.

Human society has learned "the hard way" that taking a partial dose (or missing doses) of an antibiotic is significantly less desirable than not having taken the antibiotic altogether. Low concentrations of antibiotics serve to promote resistances to these chemicals by the target organisms. Not surprisingly, then, bacteria that make antibiotics carefully control the timing of antibiotic production. That is, they have evolved a mechanism(s) to ensure that they deliver a significant dose. Cells avoid making antibiotics when their populations are meager, waiting instead until after they have grown to a sufficient population density to be able to deliver a potent dose into their surroundings. These bacteria can not see or hear, but they are able to sense each other. They can sense an increase in their own numbers, and this is called **quorum sensing**. They achieve this by producing and monitoring the local accumulation of dedicated signaling molecules.

- If these signals were entirely stable, they would fail to serve as effective proxies of population density. Over time, the environment would become saturated with the signals, and a small population would mistakenly perceive themselves to be occurring as a dense population. The desired control of antibiotic production would be lost –the antibiotics would be produced prematurely.

- If these signals were unstable to the point that they did not accumulate at all after being produced, a dense population might not recognize that it had achieved a "quorum". The desired control of antibiotic production would be lost –the antibiotics would not be produced at all.

- Not surprisingly, the signals are moderately stable, depending on the prevailing environmental conditions. The signals are *chemically* less stable at high pH, more so at low pH. The pH in the environment can vary over a very wide range, and is often dynamic, changing over time due to the metabolism of microbes.

- These signals can also be degraded *biochemically*. Some bacteria can degrade their own signals, presumably this ability would need to be tightly controlled. Other bacteria can degrade their competitor's signals, presumably in an attempt to circumvent antibiotic production.

1) How might or should a signal-producing organism balance several issues of environmental dynamics, such as issues of growth rate, population density, signal production rate, ambient pH, and signal decay (chemical and biochemical, over both long and short periods), *i.e.* to effectively control the timing of antibiotic production.

2) How might the "antibiotic target species" attempt to disrupt its competitor's communications? How might this be influenced by dynamic issues of growth rate, population density, and the capacity of an individual cell to degrade a quorum signal?