Mark Garcia
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Weiss R and Knight TF Jr. *Engineered Communications for Microbial Robotics*. A. Condon (Ed.): DNA 2000, LNCS 2054, 1-16. 2001.

Introduction

In this paper, the authors look at biological processes, that is the formation of complexes as well as the functioning of cells and their components, and compare them to the components of computer systems. Hypothesizing that the two can be intertwined, and that some of the cellular functions would benefit from aspects of computer science, they decide to implement their techniques on a single biological aspect: cell to cell communications. To do this they take a signaling system of a single chemical (*Vibrio fischeri* autoinducer) from *Vibrio fischeri*, and use it as their template for creating a system of cells wherein one actively sends a signal and the other actively receives it.

Methods

In order to create this system of sending and receiving messages, the authors first had to analyze the pathway that existed in *Vibrio fischeri*. They found that in this pathway, VFI is transcribed from the gene LuxI. This is important because this gene will need to be inserted into the plasmid that the authors create to send the messages. In addition to this, they also found that LuxR is the gene responsible for receiving the message, and binding to the DNA to send the response. So with these two important components of the pathway, the researchers created three distinct types of plasmids, preliminary ones, one with LuxI inserted in it, and one with LuxR inserted in it. The preliminary plasmids were all constructed as potential carriers of the sending and

receiving genetic material, and contained promoters and expression vectors that were needed to yield the later results of the experiment. With each advancement of the preliminary plasmids a new site of importance was added to the genetic material to make it better prepared to serve its purpose. These components included a p-(LAC-cons) so that the proteins can be transcribed, and a site of termination of transcription so that once transcription has begun, the plasmid is not caught in a never ending loop. To verify that p-(LAC-cons) was working properly, a region coding GFP was located right after it so that fluorescence could make it possible to observe expression. By placing GFP after a constitutively active promoter, the authors were able to determine from the expressions levels of GFP that the gene was in fact expressed constitutively. Sender plasmids were also constructed, with the LuxI protein's site under the control of a lac promoter. The two plasmids of great interest were PROTEt, which would express the message when induced, and pSND-1, which placed the protein of interest in the place of GFP so that it could be constitutively expressed by the lac promoter. The receiver plasmid was constructed from pRW7-3, and the plasmid PRCV-4 was used as a control with GFP to verify that in fact the signal was being received and responded to properly. The constructed cells were then tested and the signal did in fact get sent, received and responded to.

Potential Applications

This offers many great possibilities for many different fields. Clinically speaking, this technique could in theory be used to deliver small molecule treatments to cells that were in need of them. For example, if a protein on the surface of a cancer cell is identified and it is know that it could be inhibited by a particular substrate that would not

do any harm to normal cells, cells that produced that substrate could be inserted into the tissue and induced so that the growth of the tumor is actually hindered. However, while the benefits may seem limitless, at this current time there are some limitations to this method. For instance, currently the model that is used is one wherein both the signaling cells and the receiving cells contain genetic material that was completely engineered in a laboratory. In order for this technique to be effective *in vivo* there will need to be a way for the cells that are implanted into the body to both be accepted and communicate effectively with the rest of the body. There is also the question of how many of these cells could be implanted into the body because lower numbers may not be effective enough, but numbers that were too high could also have negative side effects. Ultimately in order to see what clinical possibilities this technique may have more research will first have to be done in the form of clinical trials.

From an engineering standpoint this is exciting because it again is another way in which biological systems appear to be me very similar to many concepts studied in the field of engineering. Since the authors have found a way to communicate transfer a signal from one cell to another, there is the hope that this idea could in theory branch out to further blending the two fields. For example, perhaps signals could be sent from machines and recognized by cells and vice versa. This would (in theory) or could at some point increase the number of treatments for paralysis victims given the fact that nervous tissue is incredibly difficult to regenerate.

Problems that could come along with the methods discussed here include errors in signaling. For instance, signals sent at inappropriate times in the body can lead to cells dividing at the wrong moment which in turn causes chaos in the cell cycle. This can in turn lead to cancer. Other than this concern, general errors in signaling could elicit

natural responses (immune, inflammatory, etc.) at the wrong times, and lower the quality of life for the patient being treated. In the engineering aspect of things, incorrect signaling could result in a decrease in productivity should this method simply be used as a production line of some sort, or it could also just yield false positive results which would mean a loss of time and money.

Which application demands lower error rates?
For which system is it more of a challenge?