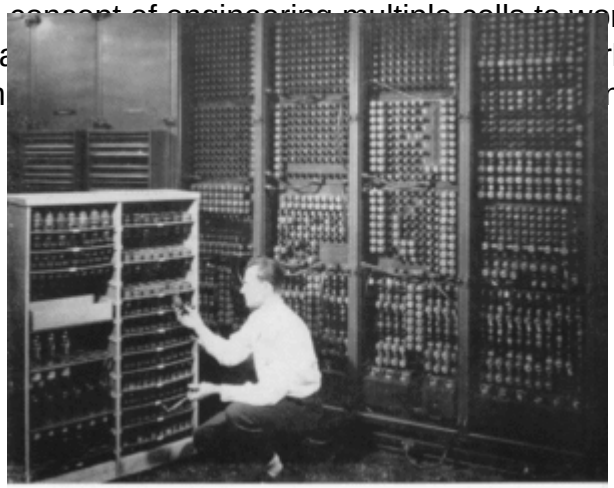
Synthetic biologists developing cells programmed to target, destroy cancer

What sort of mental imagery does the term ‘synthetic biology’ conjure up for you? No doubt someone or something very high-tech reminiscent of a character or technology from *Star Trek*. Maybe your mind goes to something more sinister like something from the *X-Files*. Or perhaps you think of something more terrestrial like the *Indominus Rex* hybrid (and others) that terrorized the park in *Jurassic World*.

However, in reality, synthetic biology covers a range of activities — all of which are to artificially manipulate biological processes to do new things and almost all are far more benign than you’ll see at the cinema. Up until recently, the current state of synthetic biology was very pedestrian — harnessing and engineering individual cells to do what we want. The most notable example was when co-opted bacteria were used to produce insulin for diabetics. But new technologies and advances have expanded the potential applications and possibilities of synthetic biology which could lead to developing systems where multiple cells are programmed to work in unison to cure a disease.

Still taking some babies steps

The concept of engineering multiple cells to work in unison is still in its early stages and it is meta rly computers and computer coding. In the early days of com nitial questions of, ‘Can we make a system that can reliably

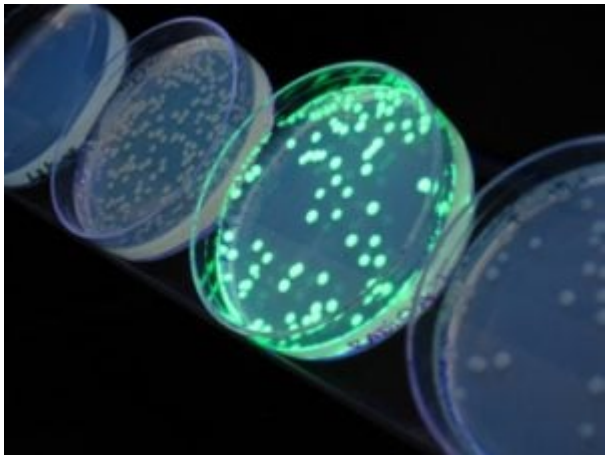


Replacing a bad tube meant checking among ENIAC's 19,000 possibilities.

and repeatably perform on/off (I/O) logic? How do we do that?

Then what?’

Researchers at Rice University in Houston, Texas have created two populations of *Escherechia coli* (*E. Coli*); one which produced a type of activator signaling molecule (a molecule that triggers action), and another group which produced a corollary type of suppressor signaling molecule (one that counteracts the first). These two molecule types would be the biological analogs of (I/O) in a computer. When puttogether, the two groups of *E. coli* would perform a relatively complex exchange where the 'activators'would trigger the 'suppressors' to produce their protein, which would then turn off the activator molecules.Representing the next step in the evolution of the concept, the team also bio-engineered the *E. coli* tofluoresce in a way that was dependent upon the strength of the cell signaling.



E. coli modified to fluoresce

This research was published in *Science*, in it the team found that "the two strains generated emergent, population-level oscillations only when cultured together." This is a fascinating result, and gives measures of the level of communication occurring between the two *E. coli* strains. They also found a certain periodicity to the fluorescing oscillations, occurring in such a way that it would build up about every two hours, and then fade again. This could be an indication that something deeper is going on within the communicating populations of bacteria that the scientists aren't aware of yet or measuring, or it could just be an artifact of the biological system itself and its internal limitations and processes. In humans there is periodicity associated with how pancreatic beta cells produce insulin, which may have as much to do with cellular communication as with the mechanics of the production and secretion of the hormone itself.

Though these interactions could be used for an incredible diversity of applications, including signaling and monitoring for tissue or bone growth, hormone production and regulation, etc., the most frequently-mentioned use in industry discussions is around disease modification.

Better disease-fighting starts with better communication

There have long been battle analogies applied to immune responses in human health — just think about the term ‘disease-fighting.’ Just as a battlefield requires reconnaissance to plan tactical activities, proper immune response requires the body to be able to understand what the pathogens and associated antigens are, and where they are. Deploying B and T cells to eliminate the threat requires that they be in the right places; It doesn’t matter if you have the most advanced warplanes in a battle if they’re in the wrong place.

A novel solution in this area has come from Matthew Chang and others who are engineering probiotics (considered to be healthy bacteria) to be able to actively seek-out and destroy pathogens within the digestive tract. But this line of thinking isn’t reserved for infectious diseases. Similar lines of scientific inquiry and research are leading to cells which can actively detect and seek out cancer cells, then be signaled to release a targeted drug. Joshua Leonard, a professor of chemical and biological engineering at Northwestern University, explained, “you might want your engineered cells to figure out whether they are sitting next to a tumor or not – and if so, release a drug.”

To fully harness all that interactive systems of living cells have to offer in terms of preventing or modifying disease — or improving health — will need to take advantage of multicellular communication. This would allow groups of cells to be able to have broader visibility into what’s occurring within the body, and produce signals for action accordingly.

Risks

What is still not studied is how this will all function under a variety of circumstances and in particular in the human body. One of the most important concepts in immunology is that the immune response is *proportional.* If it’s not strong enough, the pathogens can spread too fast and lead to significant disease or death, but if the immune response is too strong, the rebound effects can cause autoimmune problems where the body’s immune cells attack healthy ‘self’ tissues.

Properly mitigating and controlling the extent and nature of the multicellular interactivity is very likely enormously difficult to do, but will be absolutely necessary if this is to lead to viable healthcare solutions for treating diseases and disorders. This truly is one of the avenues of the future of medicine, expect a great deal more to come out on this topic in the months and years to come.

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