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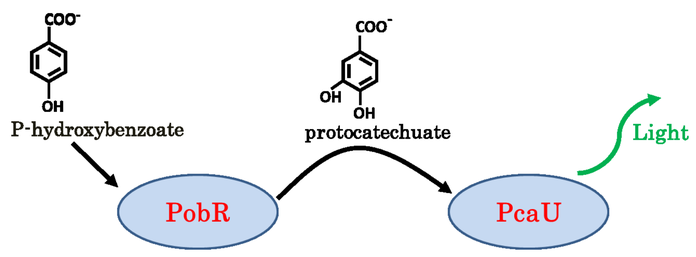
Metabolic Wiring

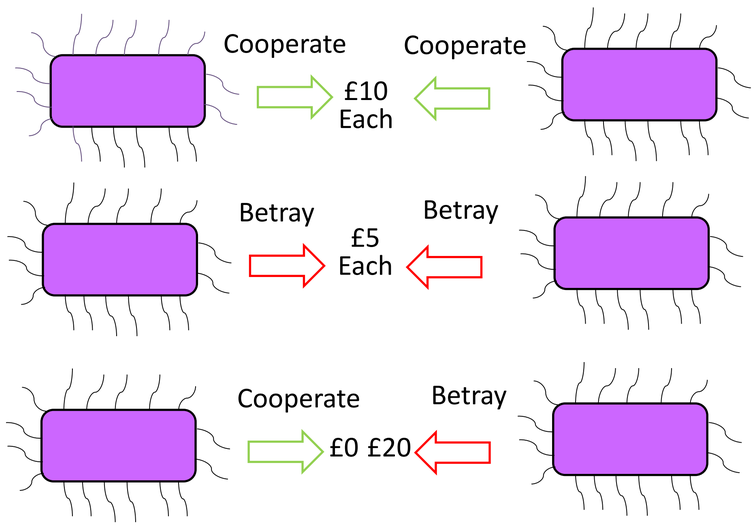
We are introducing a newly discovered cell-cell communication method to iGEM, called metabolic wiring. This uses intermediate metabolites of a pathway as the signalling molecules. Our aim is to establish this new orthogonal signalling mechanism for the synthetic biology community. To demonstrate its potential, we are using MW to build a complex circuit in the Iterated Prisoner's Dilemma game.

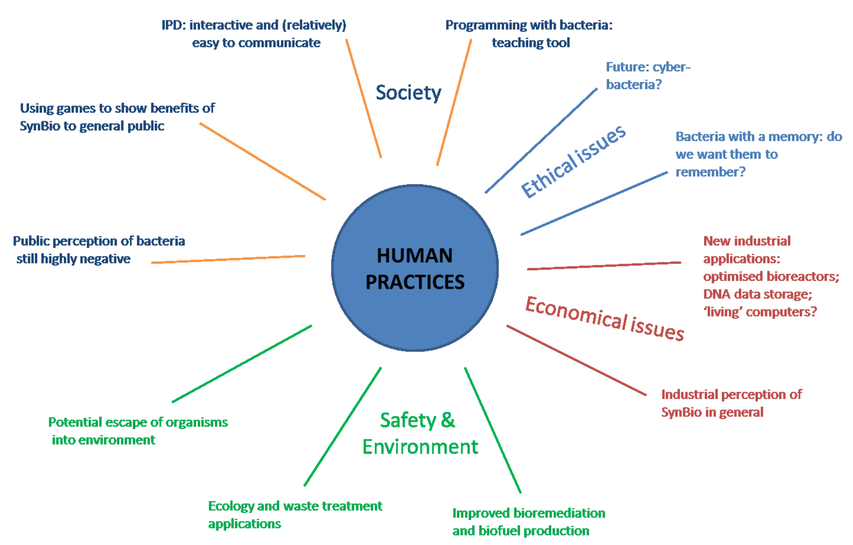


Regulatory protein	Reaction	Gene
PobR	p-Hydroxybenzoate into protocatechuate	pobA
PcaU	Protocatechuate into acetyl CoA and succinyl Coa	pcaIJFBDKCHG
BenR	Benozoate into catechol	BenABC
PcaV	Catechol (or protocatechuate) into acetyl CoA	pcaH

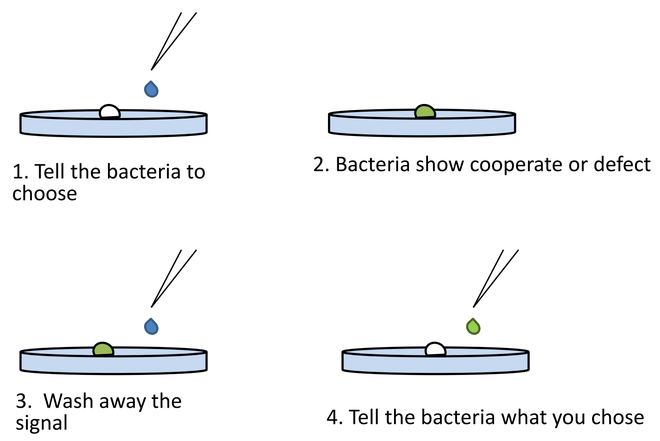
Iterated Prisoner's Dilemma

We intend to make an interactive demonstration of biological circuits, by designing bacteria that can play a game both against each other and against humans. In the game, Iterated Prisoner's Dilemma (IPD), players have the choice to cooperate or betray the other player for a varying reward. We have recreated four simple strategies from logic gates.

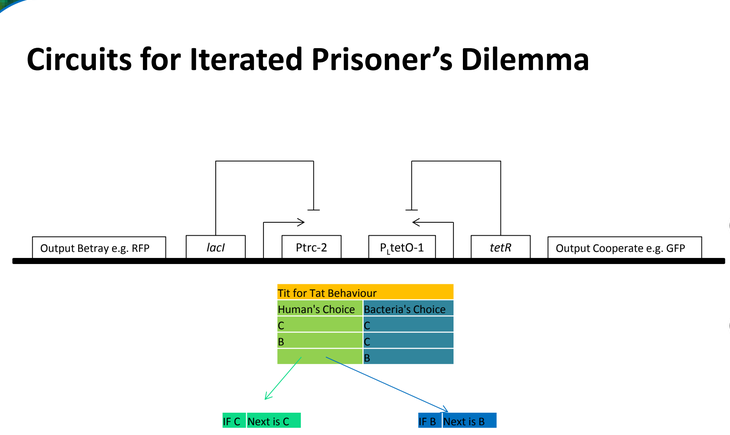




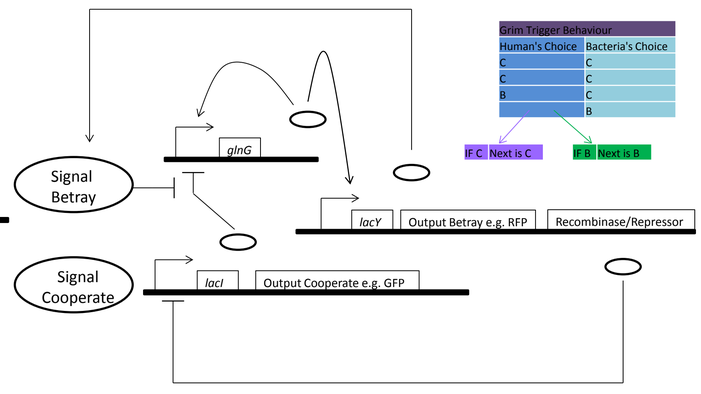
How to play iterated prisoner's dilemma against a bacterium



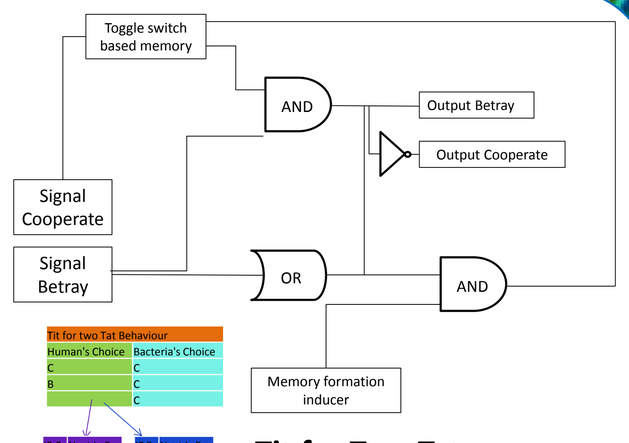
Circuits for Iterated Prisoner's Dilemma



Tit for Tat



Grim Trigger



Tit for Two Tat

Modelling and Software

The two major aspects (population control and the prisoner's dilemma) will require two different modelling techniques. The prisoner's dilemma can partly be modelled as a logical circuit, but also requires a biological oscillator (to manage iterations), for which there are many pre-existing models available using sets of ordinary differential equations. There are many pre-existing pieces of modelling software available to us, including the open-source Kappa Simulator, allowing for us to easily run full simulations of our models. Modelling will particularly important for determining the stability of the population control system.

References:

Silva-Rocha R and Lorenzo V. (2013). Engineering Multicellular Logic in Bacteria with Metabolic Wires. *ACS Synthetic Biology*. 3 (1), 204-209

Metabolic wiring: future applications

One of the many future applications enabled by this technology, is a system for regulating the composition of a mixed culture. By using the population sizes of two strains as the inputs for regulating the growth of the third strain, we could theoretically achieve a steady state, where all three populations are present in the exact proportions that we define. In this figure, each strain is represented by AND gate, the output of which is its own population size.