Project title: Game theory with viruses and the spontaneous evolution of cooperation

Supervisor: Professor Alfonso Jaramillo

Introduction
Game theory is concerned with the interactions of individuals that adopt conflicting strategies. It postulates that the rules of the game can be formulated and solved using mathematics in order to determine which strategy will prevail. Evolutionary game theory suggests that if all individuals in a population select the ideal fitness strategy within a niche, then no individual employing a non-conformist strategy can outcompete the remainder. If neither strategy supplants the other entirely, then, the two strategies will co-exist. However, an individual's fitness payoff can vary, according to whether individuals in the population are using a certain strategy, or according to how often that individual faces a specific frequency-dependent fitness. In mathematical models for the adaptation and co-evolution of genomes in biological populations, the fitness-maximizing outcome can include oscillations and chaos. Game theory is useful for analysing frequency-dependent selection [1].

Objectives
The objective of this project consists of designing strategies where natural selection can lead to cooperation[2]. The student will model an ecosystem of bacteriophages (viruses of bacteria) and their bacterial hosts, where they will compete/cooperate for resources. This will require a model with delay differential equations[3] together with the incorporation of DNA information[4,5]. Evolution will act at the DNA level by mutation and recombination. The proposed modelling will allow proposing novel experiments.

Importance
Many scales of biological organization require cooperative interactions, from single cells to ecosystems. Human society is based on cooperation.

Background to be assimilated and techniques required
The student will be assumed to be familiar with game theory and programming. The student will learn applications aimed at re-engineering living bacteria. He/she will interact with researchers involved in experimental molecular biology, directed evolution, 3D printing and Arduino.

Deliverables
Software to simulate the infection of bacteria by several species of bacteriophages, as well as the simulation providing predictions that could be tested experimentally in our lab.

End users
Evolutionary game theory has applications going from animal behaviour and ecology to speciation, macroevolution, and human language.

Follow-up PhD project
The proposed research will be extended to an experimental validation in living cells. This will require learning experimental molecular biology, microfluidics, and quantitative live cell imaging. This work will be done in collaboration with international collaborators (Harvard and MIT).

References
1. Nowak, M. A. & Sigmund, K. 2004 Evolutionary dynamics of biological games. *Science* **303**, 793–799. (doi:10.1126/science.1093411)
2. Nowak, M. A. 2006 Five rules for the evolution of cooperation. *Science* **314**, 1560–1563. (doi:10.1126/science.1133755)
3. Cairns, B. J., Timms, A. R., Jansen, V. A. A., Connerton, I. F. & Payne, R. J. H. 2009 Quantitative models of in vitro bacteriophage-host dynamics and their application to phage therapy. *PLoS Pathog* **5**, e1000253. (doi:10.1371/journal.ppat.1000253)
4. Rodrigo, G., Landrain, T. E. & Jaramillo, A. 2012 De novo automated design of small RNA circuits for engineering synthetic riboregulation in living cells. *Proc Natl Acad Sci U S A* **109**, 15271–15276. (doi:10.1073/pnas.1203831109)
5. Carrera, J., Elena, S. F. & Jaramillo, A. 2012 Computational design of genomic transcriptional networks with adaptation to varying environments. *Proc Natl Acad Sci U S A* **109**, 15277–15282. (doi:10.1073/pnas.1200030109)

Resources required
The lab is well funded and the students have all the support of postdocs, PhD students and technicians. I will personally meet daily with the student.