Offre de Thèse\ PhD offer

Modélisation de l'évolution de la résistance aux antibiotiques

Modeling the evolution of antibiotic resistance

Mots-clés: Modélisation mathématique, résistance aux antibiotiques, adaptation rapide, plasmides, théorie des processus de branchements

Key words: Mathematical modeling, antibiotic resistance, rapid adaptation, plasmids, branching process theory

Domaine: Génétique des populations, maladies infectieuses, théorie des probabilités

Année universitaire: 2018–2021

Date limite de candidature: Mai 15

Date de début de la thèse: négotiable; position est disponible immédiatement

Ecole Doctorale: assocation avec l'Ecole Doctorale "International Max Planck Research School (IMPRS) for Evolutionary Biology" n'est pas obligatoire mais possible

Etablissement d'inscription du/de la doctorant(e): Université de Kiel or Université de Lübeck, Allemagne

Spécialité: Evolution, Ecologie

Unité de recherche: Department of Evolutionary Theory, Max Planck Institute for Evolutionary Biology, Plön, Allemagne

Type de financement: Financement par la Société de Max Planck

Etat du financement: Obtenu

Précisions sur le financement: Contrat de 3 ans

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Co-Directeur de thèse: une comité de thèse appropriée sera composé selon les intérêts de l'étudiant(e)

Pour postuler à cette offre

Envoyer par email avant le 15 mai 2018 une Lettre de motivation + un CV + un relevé de notes de Master + deux contacts pour des Lettres de recommendation en spécifiant dans le sujet du courriel *"candidature offre de thèse 2018"* à uecker@evolbio.mpg.de.

Context

The WHO estimates that antibiotic resistant bacteria are responsible for 25,000 deaths per year in the European Union (WHO Fact Sheet "Antibiotic resistance", October 2015). Resistance to new antibiotics usually evolves quickly. At the same time, the rate of discovery of new antibiotics is decreasing. It is hence of great relevance to understand which circumstances hamper the emergence and spread of resistant strains, while successfully eliminating the sensitive bacteria. With this knowledge, we can hope to be able to tailor treatment strategies accordingly.

From an evolutionary perspective, the evolution of resistance constitutes a prime example of (undesired) evolutionary rescue (Gonzalez et al. 2013, Alexander et al. 2014). By evolving resistance, the pathogenic bacterial population rapidly adapts to the novel environmental conditions, escaping extinction and preventing patient recovery.

Project

Clinically relevant resistance is often encoded on plasmids. Plasmids are extra-chromosomal DNA elements that are passed on from the mother cell to the daughter cells. In addition, many plasmids can horizontally transfer from one cell to the other. This transfer can also happen between cells of different bacterial species. Plasmids do not carry essential genes, i.e. genes that the bacterium needs to grow and to replicate. They are frequently depicted as parasites that infect and exploit the bacterial cell, imposing a cost on its host. However, in the presence of antibiotics, plasmids carrying resistance genes turn from a burden into a life-saving asset. The location of resistance genes on plasmids can lead to special evolutionary dynamics, different from those of resistance genes on the chromosome. Yet, most mathematical models focus on chromosomal resistance, leaving the dynamics of plasmid-borne resistance under-explored.

The goal of this project is to develop a set of mathematical models to explore the special role of plasmids in the evolution and maintenaince of antibiotic resistance. Specifc topics could concern

the copy number of the plasmid within the bacterial cell or the commensal flora as a reservoir of resistance genes.

Methods

On the mathematical side, the project will be mainly based on branching process theory, complemented by the analysis of deterministic ODE systems and stochastic computer simulations. Branching processes are a special class of stochastic processes in which individuals reproduce independently from each other. This property allows for the derivation of many beautiful analytical results. In population genetics, branching process theory provides a versatile tool to determine the establishment probability of beneficial alleles. In the thesis, the student will use time-inhomogeneous and multi-type branching processes to describe the establishment process of the resistance plasmid. Overall, the project will be situated within the modeling framework of evolutionary rescue (Orr & Unckless 2008, Martin et al. 2013, Uecker et al. 2014, Uecker & Hermisson 2016, Uecker 2017, Anciaux et al. in press).

Institution

The student will join my recently established group within the Department of Evolutionary Theory at the Max Planck Institute for Evolutionary Biology. Through the department, the student will be part of a larger group of scientists, offering the opportunity for discussions, the participation in group meetings, journal clubs, reading groups etc. The working environment is international and welcoming and offers an excellent infrastructure. Funding for the attendance of conferences and workshops is available.

Besides theoretical biology, research at the institute spans evolutionary genetics, evolutionary ecology, and experimental evolution. With the close-by Universities of Lübeck and Kiel and the Kiel Evolution Center, the institute is embedded into a collaborative scientific community. Depending on the student's background and the focus of the thesis, the doctorate will be awarded by the University of Lübeck (mathematics) or the University of Kiel (biology).

Association with the International Max Planck Research School (IMPRS) for Evolutionary Biology is possible. This would offer opportunities for further training such as short lab exchanges within the working groups of the IMPRS.

Profile

I am looking for a motivated student who has a keen interest in mathematical modeling as well as in biological systems. This PhD thesis requires good quantitative skills and familiarity with the characteristics of plasmid-borne antibiotic resistance or an interest in acquiring this knowledge. Prior experience in mathematical modeling and knowledge of a programming language (C, C++, Java, R, Python...) is an advantage.

The candidate should be curious, reliable, and have good communication skills, enabling him/her to collaborate in a team. The working language is English. Knowledge of German is not required.

References

Alexander H. K., Martin G., Martin O. Y., Bonhoeffer S., 2014 Evolutionary rescue: linking theory for conservation and medicine. Evolutionary Applications 7: 1161–1179.

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Gonzalez A., Ronce O., Ferriere R., Hochberg M. E., 2013 Evolutionary rescue: an emerging focus at the intersection between ecology and evolution. Philosophical Transactions of the Royal Society B Biological Sciences 368: 20120404–20120404.

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Tazzyman S., Bonhoeffer S. 2014 Plasmids and evolutionary rescue by drug resistance. Evolution 68(7): 2066–2078.

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