Proposition de recherche doctorale

Emergence et évolution des agrégats (micro)biologiques : rôle de la taille des groupes et du processus d'agrégation

Mots clés :

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- **Unité de recherche** : Unité de modélisation mathématique et informatique de systèmes complexes
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Résumé du projet de recherche (Langue 1)

Keywords: group size, aggregation, agent-based models, emergence of cooperation, collective behavior --- {{{Introduction}}} Questions. Ensembles of cells displaying coordinated behaviours and an internal homogeneity are the fundamental brick constituting multicellular organisms. Although not as organised as tissues in multicellular life forms, microbial aggregates often stand as individual recognizable units, to the point that the border between unicellularity and multicelluarity is sometimes blurred. For instance, bacterial cells communicate through quorum sensing mechanisms [Waters] and are often found in multispecific 'supercolonies' called biofilms. Eukaryotes are also known to be able to estimate population density [Wuster], a particularly striking example being the complex life cycle of Dictyostelium species, consisting of an alternation of unicellular and multicellular, differentiated, phases [Jang]. In order to be recognized as 'individuals', cellular aggregates need to display a certain regularity in their size and shape, which is often conserved within the same species and the outcome of a strict regulation. The macroscopic features of aggregates depend on the one side on individual properties such as the interaction strength and the propensity to sociality, on the other it is subjected to selection from the environment. Therefore, the question of aggregate size or density evolution involves two different biological and temporal scales, one dealing with the mechanistic processes of aggregation, the other one involving the function and long-term survival of the population. Aggregate size is primarily regulated by the interaction rules among different individuals, determined for instance by physical constraints on adhesion, signalling molecules, intracellular dynamics [Bonabeau, Gomer], and such rules are themselves subjected to mutations introducing new strategies in the population. The main question addressed in this thesis is: How is the distribution of aggregate size determined, both in terms of mechanistic processes and in terms of the evolutionary history? Particular issues of this general problem are: -# How do interaction rules affects aggregation and the aggregates' sizes? -# What is the spectrum of possibly achievable aggregate sizes given some interaction rules? -# How evolutionary pressures for group cohesion affect back size distributions? {{{State of the art}}} The emergence of multicellular organisms is a fundamental step of the complexification of living forms in the course evolution. The evolutionary stability of multicellular assemblages is however questioned on the basis on the internal conflicts that may arise among the components of a whole. Such diverging interests are expected to be present at the level of cells composing a multicellular organism, as well as that of individuals composing societies. The evolution of multicellularity therefore stands together with the evolution of cooperation in the formal framework of game theory, whose particularly relevant instances are n-players games (where n is the players group size). Within this framework, explicit conditions have been evidenced for the evolutionary stability of cooperative assemblages in terms of costs and benefits for the individual units composing the aggregate [Nowak 2006]. Several hypothesis have been discussed on the necessity of additional mechanisms to promote cooperation, and notably those related to the knowledge and communication of the individual strategic choices: 'green beard' [Jensen 2006], 'reputation' [Suzuki 2005], 'punishment' [Boyd 2003]. Other hypothesis, based on the existence of alternative states than 'cooperators' and 'defectors', lead to nonequilibrium dynamics reminiscent of co-evolutionary red-queen oscillations [Hauert 2002]. Although the role of group size has been long recognised as an essential determinant of the stability of cooperative acts, small groups being more prone to cooperation than big ones, only few authors have addressed the evolutionary origin and determinants of group size [Aviles 1999, 2002]. These general game-theoretical models have often focused on the economic interaction among organisms, such as humans, with developed cognitive capabilities, and their application to the microbial world is not straightforward. Models that explain the evolution of coordinated behaviour in microbs rely on specific hypothesis on the genetic uniformity of aggregates [Brown], or on the 'discovery' of new solutions, such as somatic and germ line differentiation, that solve conflicts arising among selfish cells. Moreover, these models typically neglect the way in which groups form. Dictyostelium is a perfect model organism for this study, since it has been the subject of a thorough genetic and molecular characterization, including the recent development of single-cell measure techniques [Gregor], its cell-cell interaction dynamics has been largely addressed both experimentally [Lee] and theoretically [Lauzeral], and it has been chosen as a model organism for the experimental study of cooperation [Strassman]. {{{Project outline and motivation of the collaboration}}} This interdisciplinary project proposes to tackle the problem of group size evolution from two points of view. A top-down approach, mainly developed in Paris, will consist in analysing the conditions for the establishment of cooperation in the context of evolutionary game theory, where group size preference will be considered as an evolving trait. In parallel, a bottom-up study will be conducted in collaboration with Brazil, aimed at pinpointing what individual-level features in the interaction among microrganisms are crucial for determining the aggregation patterns observed in different microbial species, and how do this reflect in the distribution of group sizes within one species. These two issues will be primarily thought to be applied to the biological system D. discoideum. The collaboration between the French and Brasilian sides will allow to exploit complementary skills for addressing the complex dynamics of interacting cells by a combination of a biological and a computational-physical standpoint. The group at the dept. of biology of ENS will provide the expertise in nonlinear approaches to

evolution and to the dynamics of biological populations. In particular, a game-theoretical approach has already been developed in the course of a master Thomas Garçia has performed under the supervision of Silvia De Monte. Theoretical results will be compared to experiments on D. discoideum currently studied in this lab. We will dispose of movies on different strains of Dictyostelium marked with fluorescent reporters (developed by Clément Nizak, Grenoble), that will allow us to quantify for the first time the size distribution of amoebae's aggregates. Moreover, we will dispose of D. discoideum strains co-evolved with bacteria in an experiment by Sandrine Adiba, and we could test the correlation between fruiting body size and the nature of the bacterial aggregation (evolving towards biofilm formation). The group at the dept. of Physics of Porto Alegre has a long-standing experience in modelling 'active fluids' and has recently become very interested in biological applications. A numerical model developed by L. G. Brunnet and D. Calovi, describing Dictyostelium aggregation in terms of self-propelled particles endowed with an intracellular dynamics, will allow us to efficiently test the importance of physical factors such as the attachment and fission properties, the signalling strategies and the initial spatial repartition on the aggregate size. {{{Expected results and perspectives}}} We expect two main points to be achieved in this thesis: -# the formulation of general conditions on the aggregation rules and on the selective forces defining the cooperative game for the evolution of the interaction in sizable groups; -# the identification of key interaction properties allowing to control the aggregate size distribution In perspective, we hope to help understanding ho the transition to multicellular life forms might have happened and why do ctain organisms keep complex life cycles where unicellular and multicellular stages alternate. This work is susceptible to be applied both to social sciences, where it may provide a new perspective on public goods games evolutionary dynamics, and to medical sciences, where an altered sensitivity to local cell density is a hallmark of metastatic tumors. {{{References}}} {{Avilés L.}} Solving the freeloaders paradox: Genetic associations and frequency-dependent selection in the evolution of cooperation among nonrelatives. Proc Natl Acad Sci U S A. 2002 Oct 29;99(22):14268-73 {{Bonabeau E, Dagorn L, Fréon P.}} Scaling in animal group-size distributions. Proc Natl Acad Sci U S A. 1999 Apr 13;96(8):4472-7 {{Boyd R, Gintis H, Bowles S, Richerson PJ.}} The evolution of altruistic punishment. Proc Natl Acad Sci USA. 2003 Mar 18;100(6):3531-5 {{Calovi D, Brunnet L.G., de Almeida R.M.C.}} cAMP Diffusion in Dictyostelium discoideum: A Green’s function method , to be published. {{Gomer R, Gao T, Tang Y, Knecht D, Titus MA.}} Cell motility mediates tissue size regulation in Dictyostelium. J Muscle Res Cell Motil. 2002;23(7-8):809-15 {{Gregor T, Fujimoto K, Masaki N, Sawai S.}} The Onset of Collective Behavior in Social Amoebae. Science 2010 328:1021-1025 {{Jang W, Chiem B, Gomer RH.}} A secreted cell number counting factor represses intracellular glucose levels to regulate group size in dictyostelium. J Biol. Chem. 2002 Oct 18;277(42):39202-8 {{Hauert C, De Monte S, Hofbauer J, Sigmund K.}} Volunteering as Red Queen mechanism for cooperation in public goods games. Science. 2002 May 10;296(5570):1129-32 {{Jang W, Gomer RH.}} Combining experiments and modelling to understand size regulation in Dictyostelium discoideum. J R Soc Interface. 2008 Aug 6;5 Suppl 1:S49-58 {{Jansen VA, van Baalen M.}} Altruism through beard chromodynamics. Nature 2006; 440(7084):663-666 {{Lauzaral J, Halloy J, Goldbeter A.}} Desynchronization of cells on the developmental path triggers the formation of spiral waves of cAMP during Dictyostelium aggregation. PNAS 1997;94:9153-9158 {{Lee KJ., Goldsein RE, Cox EC.}} Resetting Wave Forms in Dictyostelium Territories. PRL 2001; 87: 068101 Nowak MA. Five rules for the evolution of cooperation. Science. 2006;314(5805):1560-3 {{Strassman JE, Zhu Y, Queller DC.}} Altruism and social cheating in the social amoeba Dictyostelium discoideum. Nature 2000, 408: 965-967 {{Suzuki S, Akiyama E.}} Reputation and the evolution of cooperation in sizable groups. Proc Biol Sci. 2005 Jul 7;272(1570):1373-7 {{Waters CM, Bassler BL.}} Quorum sensing: cell-to-cell communication in bacteria. Annu Rev Cell Dev Biol. 2005;21:319-46 {{Wuster A, Babu MM.}} Transcriptional control of the quorum sensing response in yeast. Mol Biosyst. 2010 Jan;6(1):134-41