

synthesiology? Synthesiology English Edition, 1(4):282-290, 2009.

[8] H. Nakashima. On methodology of constructing multi-level emergent systems. In Proc. of 3rd Int. Workshop on Emergent Intelligence on Networked Agents (WEIN'09), May 2009.

[9] H. Nakashima, M. Suwa, and H. Fujii. Endo-system view as a method for constructive science. In Proc. 5th International Conference of the Cognitive Science (ICCS 2006), pages 63-71, 2006.

[10] H. Nakashima, M. Suwa, and H. Fujii. Innovaton in the framework of methodology for constructive informatics. IPSJ Journal, 49(4):1508-1514, 2008. in Japanese.

[11] H. A. Simon. The Sciences of the Artificial. MIT Press, Cambridge, Massachusetts, third edition, 1996.

Oct. 16 (Fri.) 13:30-14:10

Macroscopic relationship among robustness, evolvability, and phenotypic fluctuations

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Characterization of biological plasticity, robustness, and evolvability in terms of dynamical systems and statistical analysis is an important issue in Complex Systems Biology. First, proportionality among evolution speed, phenotypic plasticity, and isogenic phenotypic fluctuation is derived as an extension of fluctuation-response relationship in physics. Following an evolutionary stability hypothesis we then derive a general proportionality relationship between the phenotypic fluctuations of epigenetic and genetic origin; The former is the variance of phenotype due to noise in developmental process, and the latter due to genetic mutation. The relationship suggests a link between robustness to noise and to mutation, as robustness can be defined by the sharpness of the distribution of phenotype. Second, the proportionality between the variances is demonstrated to hold also over different phenotypic traits, with which a measure for phenotypic plasticity is proposed. The obtained relationships are confirmed in models of gene expression dynamics, as well as in laboratory experiments. Third, evolutionary restoration of plasticity is investigated both theoretically and experimentally in terms of fluctuations.

Based on the results, we revisit Waddington's canalization and genetic assimilation, and discuss how consistency between evolutionary and developmental scales constrains robust developmental process and leads to universal laws on phenotypic fluctuations.

References: K.K. *Life: An Introduction to Complex Systems Biology*, Springer (2006); *PLoS One*(2007) 2 e434, *J Biosci*.34 (2009) in press: Ito et al., *Mol. Sys. Biol.* 5 (2009) 264

Oct. 16 (Fri.) 14:10-14:50

How Microbes Evolve to Dodge the Membrane Disruptive Actions of Antimicrobial Peptides

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Antimicrobial peptides (AMPs) kill bacteria by forming pores that increase membrane permeability to ions or larger molecules. It has been proposed that AMPs selectively disrupts microbial membranes over mammalian membranes. The question remains as to why microbes have not been more successful in resisting the activity of AMPs. As the target of antimicrobial peptides is the plasma membrane, a microbe would have to redesign its membrane, changing the composition and/or organization of its lipids to dodge the action of AMPs. This is likely to be a 'costly' solution for most microbial species. Yet, over the years, some pathogens have successfully developed countermeasures to limit the effectiveness of AMPs, allowing them to survive in the presence of AMPs that would have otherwise killed them. Here we explore the factors involved in antimicrobial resistance. To get at the mechanism of action of AMPs, we directly visualize the topological changes induced by AMPs in model membranes via atomic force microscopy (AFM). AMPs induce structural transformations in supported lipid bilayers, progressing from fingerlike instabilities at bilayer edges, to the formation of surface-defects, and finally to a network of stripe-like structures in zwitterionic model membranes with increasing PG-1 concentration. While zwitterionic bilayers exhibit surface defects with the addition of AMPs, surface defects are not observed as an intermediate stage of membrane disruption in anionic lipid membranes. These and other results obtained from lipids with different chain length indicate that lipid compositions, lipid fluidity and hydrophobic mismatch between AMPs and acyl chains of the lipid bilayer all play important roles in antimicrobial resistance.