Robustness Mechanisms in Biology

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Robustness is an important concept within the biological world. We might define it by the *small variance of a state* of the subject, e.g. health, fitness or phenotype, *against changes in the underlying working conditions* compared to the variance of other possible states against the same changes.
Robustness differs from other concepts like stability and adaptivity (returning to a desired state), persistence, recovery and flexibility by its intrinsic structural components. Robustness may include topics like stability (small state perturbations lead to only small state changes) or structural stability (small structural parameter changes lead to a new system with the same qualitative behaviour), but include more aspects like organisation and architecture of a system, the offset between function, possible functional changes and architecture, and topics like the controversy between adaptivity and identity, i.e. plasticity vs. stability.

In our context we are mostly interested in mechanisms of robustness in the molecular biological world. We are interested in *phenotypic robustness*, i.e. the robustness of biological entities against changes in the underlying environmental and genetic mechanisms. There are two main robustness principles known in literature: canalization and neutrality.

- *Canalization*: During the developments of a species, phenotype variations might be suppressed. This was first formulated by Waddington [1] and can be seen as a multi-hill potential fitness landscape where a ball rolls always downhill. Although there are several possible routes, only one (the channel) with the best fitness is taken during species development. Changing environmental conditions may lead to changes in the landscape, altering the resulting phenotype. Nevertheless, the phenotypic variance in many developments will stay small.

- *Neutrality*: Although there might be huge phenotypic differences, the fitness of those phenotypes may not differ significantly and will not lead to natural selection; they are evolutionary neutral. This idea was introduced by Kimura [2][3] and first observed for electrophoretic data for a species which had a much bigger variance than expected [4].

The molecular reasons for these observations are manifold. Mechanisms are based on

- *Redundancy*: The effects of multiple copies of a gene (*paralogues* copies during replication) are buffered because doubling the function promote may not lead to higher resulting effect concentrations. This is true for transcription factors, signal transduction proteins, metabolic pathway genes and the variable genes encoding antibody peptides. Thus, the effects of mutations of the paralogues genes are buffered, leaving the original phenotype intact and providing phenotypic robustness. This mechanisms is only counteracted by its implied molecular costs which are too high for fast replicating and translating organisms like viruses and bacteria.

- *Deleterious variance suppression (anti-redundancy)*: Even if the molecular costs are not so important, high redundancy may lead to accumulation of deleterious mutations after several generations. Therefore, countermechanisms to redundancy are observed: in kernel based cells (*eukaryotes*) and multi-cellular subjects, there are checkpoint genes (e.g. p53) which enhance the damages of mutations, leading to enhanced fitness variance and therefore to selection. Other mechanisms are the decline in telomerase enzyme which limits the replication of a cell line, or the loss of key error repair genes in mitochondria which leads to a reduced rate of accumulation of deleterious mutations.

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3. Kimura M.: *DNA and the Neutral Theory*, Phil. Trans. Roy. Soc. Lond. B Biol. Sci. 312 (1154) (1986): 343-354
4. Lewontin R.C.: *The Problem of Genetic Diversity*. Harvey Lect. 70 (Series) (1975): 1-20