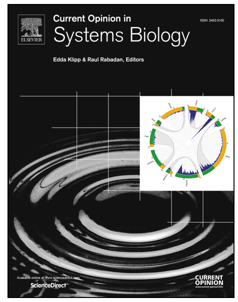

Dealing with noise: The challenge of buffering biological variability

Inna Averbukh, Avishai Gavish, Benny Shilo, Naama Barkai

PII: S2452-3100(16)30031-2

DOI: 10.1016/j.coisb.2016.12.011

Reference: COISB 11

To appear in: *Current Opinion in Systems Biology*

Dealing with noise: The challenge of buffering biological variability

Inna Averbukh*, Avishai Gavish*, Benny Shilo and Naama Barkai
Department of Molecular Genetics, Weizmann institute of Science, Rehovot, Israel

*Equal contribution
Naama.barkai@weizmann.ac.il ; Benny.shilo@weizmann.ac.il

Cells process information using bio-molecular circuits of interacting proteins and genes. A remarkable property of these circuits is their ability to function in highly variable biological environments: Biochemical processes are stochastic, environmental conditions fluctuate, and genetic polymorphisms are abundant. How is variability buffered to maintain a robust output? Can variability be exploited to allow computations not possible by deterministic dynamics? These questions lie at the heart of contemporary systems biology. We argue here that biological variability is fundamental for understanding principles underlying design and function of biological circuits. As concrete examples, we will discuss the buffering of variability during embryonic patterning, and the incorporation of variability in microbial responses to changing conditions.

Biological processes are subject to high variability at the molecular level. First, molecular interactions are stochastic, performed by a finite (and sometime low) number of molecules [1-3]. Kinetic processes are also dependent on fluctuating parameters in the external environment such as temperature or pH. Furthermore, genetic mutations or polymorphisms introduce an additional source of variability, as they could influence enzymatic concentrations or reaction rate constants. The need to operate in a *"noisy"* environment is therefore a defining property of biological systems.

In stark contrast to this high variability, key biological processes are extremely reproducible. Perhaps the best illustration of this robustness is the patterning of multicellular organisms, which remains invariable between individuals grown in widely differing conditions. This so-called *canalization* was studied since the early days of embryology [4,5]. While error compensation may occur at subsequent stages of development, or act directly to minimize the source of variability [6**], we will argue here that variability is buffered already at the level of the biochemical circuits defining the very initial stages of differentiation.