Constrains on a module's effective sensitivity by the input and readout dynamic range

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***Short Abstract* — Many features of biochemical modules should be analyzed in a proper context to gain insight into how such a component behaves under physiological conditions. Using a very simple setup we explore how the dynamic range spanned by upstream and downstream components, and the nonlinearities of a general sigmoidal-shaped module's response function could be tuned to produce effective sensitivities much less or even larger than the sensitivity associated to the original module when considered in isolation.**

***Keywords* — transfer function, ultrasensitivity, dynamical range**

I. Background

EXTERNAL and internal cues are continuously probed by cell specific molecular components in order to elaborate appropriate responses. A great deal of work has already been done in order to understand the behavior of the underlying biochemical reaction networks responsible of these capabilities [1,2]. Under a systems-level perspective, signal sensing, transduction, and information processing mechanisms can be usually analyzed in terms of interacting modules or minimal functional motifs [3,4]. In this context, the non-linearities observed in biochemical modules are key ingredients upon which non-trivial complex signal processing capabilities rest. However, even though module-based descriptions seems powerful (see for instance [5,6]), the integration of such modules with upstream and downstream components often alters the module information-processing capabilities, for example through mechanisms like sequestration of shared components [7,8] or differences in effective response dynamic ranges between consecutive modules [9]. Here, we analyze the influence of the later. Specifically, we explore how the dynamic range spanned by upstream and downstream components, and the nonlinearities of a general sigmoidal-shaped module's response function could be tuned to produce effective sensitivities much lower, or even larger, than the sensitivity associated to the original module considered in isolation.

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II. Summary of Results

We based our analysis on a characterization of several sigmoidal-shaped response functions, usually found in the mathematical description of signaling motifs. New introduced coefficients n^{low}, and n^{high} allowed us to link in a very intuitive way local sensitivities displayed at low and high input ranges, respectively, with asymmetries observed in the studied response curve. We then considered upstream and downstream components of the simplest form (i.e. Michaelis-Menten), which allowed us to define, for the analyzed sigmoidal module, an upstream-limited and a downstream-limited working regime. The effective sensitivity of this general setup depends on the relationship between spanned dynamic ranges and EC50 levels of the considered transfer functions. We further explored in detail the cases of Hill-type, and Golbeter-Koschland response functions. In these, we analyzed when and how different combination of input/output dynamic ranges and internal parameters of the respective systems result in different levels of effective sensitivities. In particular, we showed how sensitivity levels, much larger than the module original one, may be achieved for the asymmetric GK case.

III. Conclusion

In this contribution we focused on how dynamic ranges spanned by upstream/downstream elements affect effective sensitivities of modules displaying general sigmoidal response functions. We found that there exist regimes where the existing nonlinearities and asymmetries could produce an unexpected increase in the observed sensitivity levels.

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