

Conservation of Robustness: Proof of Bode's Sensitivity Integral Formula for Nonlinear Systems and Its Implications for Biology

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ABSTRACT

One hallmark of many complex systems is their “robust yet fragile” character; robust to designed-for uncertainties, and fragile to design flaws and unanticipated perturbations [2]. Bode’s sensitivity integral captures these robustness tradeoffs in a compact form. In simple terms, the formula states that reducing the sensitivity to a disturbance at certain frequencies will increase the sensitivity at other frequencies. The proof for linear systems has been attributed to Bode [1].

The main result of this work is a proof of Bode’s sensitivity integral formula for nonlinear systems. The proof depends only on the causality of the system, not linearity, making it a fundamental conservation principle. We investigated the implications of this formula for one class of complex nonlinear systems, biochemical reaction networks. First, we argue that

many types of biological oscillations may arise spontaneously as the result of perturbing pathways under tight negative feedback regulation. We use as an example a simple model of yeast glycolysis. Second, we suggest that the formula places limits on the gain of a single feedback loop, thus necessitating a more distributed strategy of control using multiple feedback loops. We illustrate this point with a simple model of vertebrate phototransduction.

REFERENCES

- [1] Bode, H. W. *Network Analysis and Feedback Amplifier Design*, D. Van Nostrand, Princeton, 1945.
- [2] Carlson, J. M. and Doyle, J. Highly optimized tolerance: A mechanism for power laws in designed systems, *Phys. Rev. E*, 60:1412, 1999.