

Applying URC Fuzzy Logic to Model Complex Biological Systems in the Language of Biologists

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ABSTRACT

Recent technological advances in high-throughput data collection give biologists the ability to study complex systems as a whole. A new methodology is needed to (a) develop and test biological models based on experimental observations and (b) predict the effect of perturbations to the network (e.g. genetic engineering, pharmaceuticals, antibiotics, gene therapy). We propose that fuzzy logic is a natural language for modeling biology.

Fuzzy models have enough resolution to accurately model complex phenomena, while not requiring the precise experimental measurement of many kinetic parameters. More importantly, fuzzy models use a mathematical framework that can be easily adapted to linguistic models currently prevalent in biology, and thus may be applied by biologists without the need for experts in other fields or "black-box" software.

Applications of fuzzy models have been limited by exponential growth in fuzzy rule bases as resolution and model size increases. The Union Rule Configuration (URC) of fuzzy logic [1] avoids combinatorial explosion in the fuzzy rule base, allowing complex system models without the need for additional domain knowledge. Thus, URC fuzzy logic can be used to efficiently learn and test models using large biological data sets, such as DNA chips and microarrays.

We demonstrate the URC fuzzy model on fundamental examples of biological regulation, including the *lac* operon of *E. coli*, the *trp* operon, the λ phage switch, and other common mechanisms of bacterial and eukaryotic gene regulation. The goal is to demonstrate the utility of URC fuzzy modeling, while simultaneously developing a theoretical basis for its universality as a function approximation for biochemical kinetics. We are also using URC fuzzy logic to help build models from experiments with whole-genome microarrays (complemented by RT-PCR and protein screening by SELDI-MS) on the virulence pathway of *Yersinia pestis*, the bacteria that cause plague, which consists of at least 40-50 (known) genes regulated by temperature and calcium concentration.

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REFERENCES

- [1] W. E. Combs and Andrews, J. E., "Combinatorial rule explosion eliminated by a fuzzy rule configuration," *IEEE Trans. Fuzzy Syst.*, vol. 6, pp. 1-11, Feb., 1998.