

Oral Presentation

NINJA: Boolean Modelling and Formal Verification of Tiered-Rate Chemical Reaction Networks

Aadithya V. Karthik^{1,*}, David Soloveichik², Sayak Ray³, Baruch Sterin¹, Alan Mishchenko¹, Robert Brayton¹, and Jaijeet Roychowdhury¹

¹UC Berkeley, ²UC San Francisco, ³Princeton University

* aadithya@berkeley.edu

We present NINJA¹, a suite of computational techniques for modelling and formally verifying properties of tiered-rate chemical reaction networks (TCRNs). A k -tier TCRN is a system composed of reactions that proceed simultaneously at k widely differing speeds/timescales. For example, a 2-tier TCRN consists of reactions that proceed at two widely differing speeds, “fast” and “slow”². It is well-known that virtually every computable function may be realized by a (suitably constructed) TCRN. Indeed, because there exist reliable and cost-effective techniques (*e.g.*, based on strand displacement cascades) for implementing arbitrary TCRNs using physically realizable molecular systems, TCRNs have become the molecular system designers’ *de facto* choice for implementing a wide range of functionality required in engineered reaction systems, including oscillators, combinational and sequential digital logic modules, amplifiers, comparators, *etc.* However, a key problem faced by the designers of such systems is *formal verification*. Because TCRNs are concurrent systems with multiple moving parts, they often contain several subtle and hard-to-diagnose bugs. Moreover, even with just a few reactions/species, TCRNs can quickly become too complex to analyze by hand; therefore, manually proving that a given TCRN realizes a given functionality (with no bugs or unwanted side-effects) is tedious, error-prone, and in many cases, completely infeasible. To address this problem, in this work, we propose an automated technique (dubbed NINJA) for formally verifying the correctness of TCRNs. Given a TCRN, NINJA first constructs a *purely Boolean model* that captures the functionality of the given TCRN. This Boolean model operates at the molecular level, *i.e.*, the number of molecules of various species are represented as bit vectors within the model. The model is also *non-deterministic* and *sequential*, *i.e.*, given the current state of the system (the molecular counts of the various species) as a bit vector, the model includes functionality for computing all possible next states of the system, taking into account the tiered structure of the underlying reactions. Furthermore, the Boolean model is encoded in a form (more precisely, as a Berkeley Logic Interchange Format, or BLIF, file) that most existing formal verification tools (*e.g.*, ABC) can take as input. Thus, the Boolean model may be used in conjunction with existing formal verification/model checking tools and techniques to formally prove the correctness of the underlying TCRN. For example, we have been able to use NINJA to formally verify a TCRN that implements a “consensus” system, which is a building block used in many engineered molecular reaction networks. We have also applied NINJA to formally upper-bound the molecular counts of species in non-trivial chemical exponentiation networks. The only drawback that we have encountered so far is *scalability*: as the number of reactions/species grows, the formal verification can sometimes become very time-consuming. We believe that specialized verification primitives can be developed to help address this issue by intelligently arresting the underlying time complexity, and we are now actively pursuing this line of research.

¹NINJA Is Not a Justifiable Acronym

²We assume that the precise values of the reaction rate coefficients in the system do not affect the system’s end-to-end behaviour; instead, all that matters is that “fast” reactions occur at much higher speeds than “slow” reactions.