

# *BetaWB – a language for modular representation of biological SYSTEMS*

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## **Extended Abstract**

With the increased interest in understanding biological networks, such as protein-protein interaction networks and gene regulatory networks, creating comprehensive models that represent, simulate and predict biological behaviours have become increasingly important. This interest has been fuelled primarily by the development of appropriate experimental and modelling tools that produces data and builds models for testing and verification. In this account, we introduce the use of Beta workbench (BetaWB)[1], a process algebra [2, 3] based formalism in depicting mechanistic biological models – such as the NF-kappaB signalling pathways. We further point up its ability to (1) model the dynamic behaviour of molecular systems – e.g. movement of molecules between different compartments such as from the nucleus to the cytoplasm and (2) compose models of diverse complementary systems in deriving more complex scenarios.

By abstracting biological systems on the level of their behaviours, models are obtained sharing many characteristics with computational engineering systems. That is to say, detailed understanding and control of biological networks requires a level of description similar to that of engineering of complex artificial systems. The aforementioned, BetaWB – is an approach for constructing models of biological networks which is based on process calculus technique. BetaWB is based on beta-binders formalism, where the molecules are modelled as  $\pi$ -calculus processes[1] *wrapped* by borders equipped with typed interaction channels that represent explicit interaction sites. Such formalism comes with a rigorous “semantics” that goes beyond the simple positive and negative interaction symbols typically used in biological diagrammatic models. BetaWB defines a reliable method for depicting the states of molecular systems as well as its evolution over time, that is, by its very nature, provides the means for tracing the dynamics of systems behaviour.

We describe the use of this formalism in constructing multi cellular models of the interaction between NF-kappa B[4, 5] and other pathways in eukaryotic cells. Through this work we demonstrate that state-based mechanistic models are particularly well-suited for capturing the level of understanding obtained using the tools; and that creating such executable biological models is indeed beneficial.

The construction of mechanistic quantitative models of biological systems with the beta binders formalism can be used in much the same way as traditional quantitative connectivity diagrams to interpret large volumes of data, design new experiments, as well as understand mechanistic details of biochemical pathways. However use of such formalisms to describe models of biological systems have the added advantage of being able to (1) represent phenomena of importance to biological systems such as time dependent, causal driven and concurrent behaviours; (2) act as formal verification methods used to ensure the consistency of the generated computational models with their biological data counterparts – i.e. by formalizing both the experimental observations obtained from a biological system and mechanisms underlying the systems behaviours, one can formally verify that the quantitative model does reproduce the systems known behaviour. Other significant benefits in constructing models using BetaWB includes its capability of composing models of diverse systems, the interplay between multiple pathways and computing the states of their evolution.

1. Priami C, Regev A, Shapiro E, Silvermann W: Application of a stochastic name-passing calculus to representation and simulation of molecular processes. *Inf Process Lett* 2001, **80**(1):25-31.
2. Bergstra JA, Ponse A, Smolka SA (eds.): Handbook of Process Algebra: Elsevier Science; 2001.
3. Regev A, Shapiro E: Cells as computation. *Nature* 2002, **419**(6905):343.
4. Ihekwaba AE, Wilkinson SJ, Waithe D, Broomhead DS, Li P, Grimley RL, Benson N: Bridging the gap between in silico and cell-based analysis of the nuclear factor-kappaB signaling pathway by in vitro studies of IKK2. *Febs J* 2007, **274**(7):1678-1690.
5. O'Dea EL, Barken D, Peralta RQ, Tran KT, Werner SL, Kearns JD, Levchenko A, Hoffmann A: A homeostatic model of IkappaB metabolism to control constitutive NF-kappaB activity. *Mol Syst Biol* 2007, **3**:111.