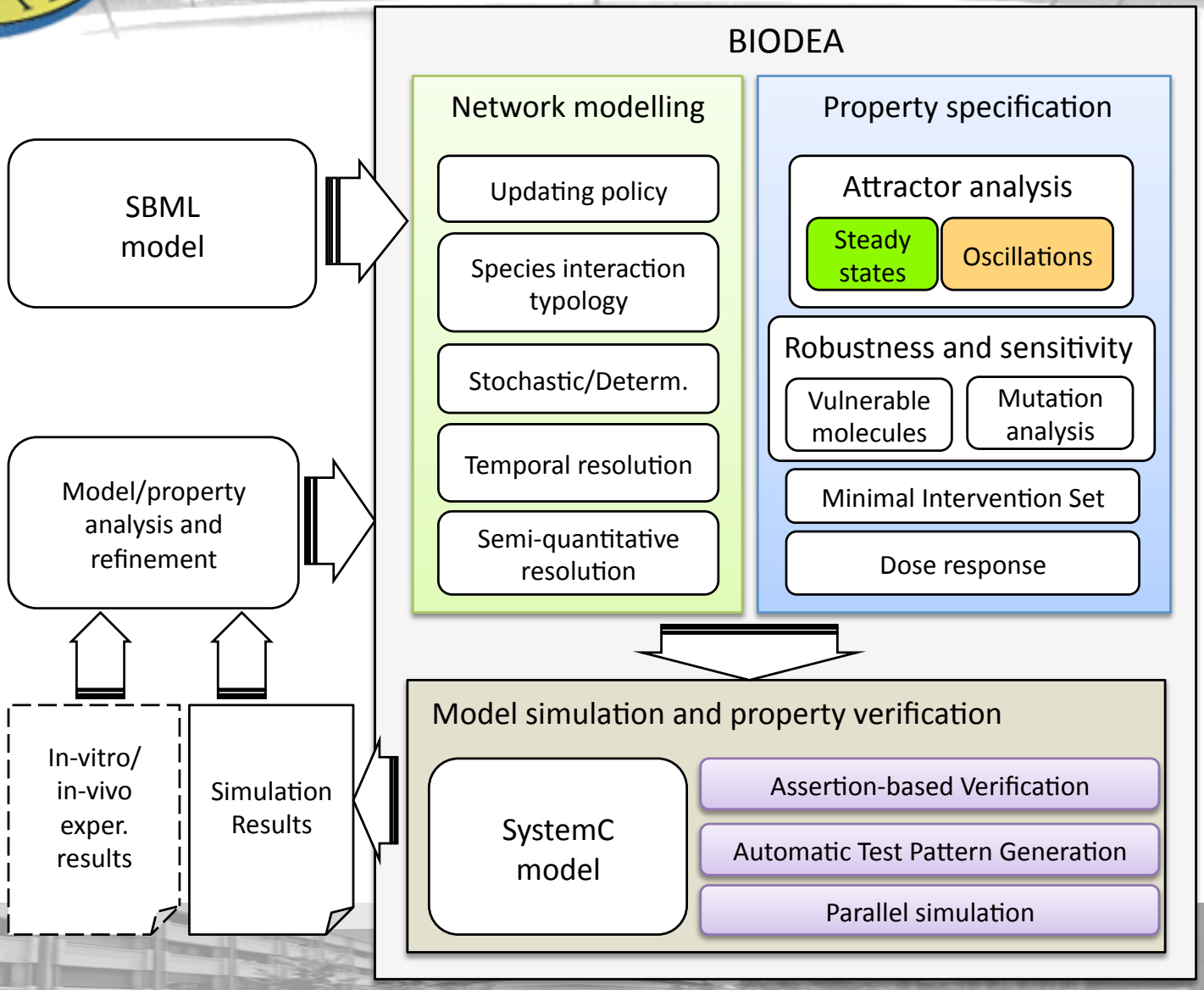
Modeling, verification, parallel simulation: from Electronic Design Automation (EDA) to Systems Biology

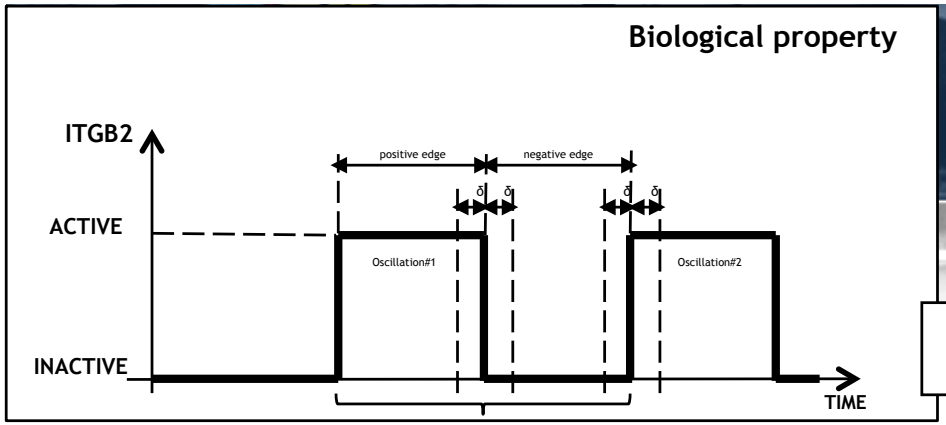
Modeling and simulation framework

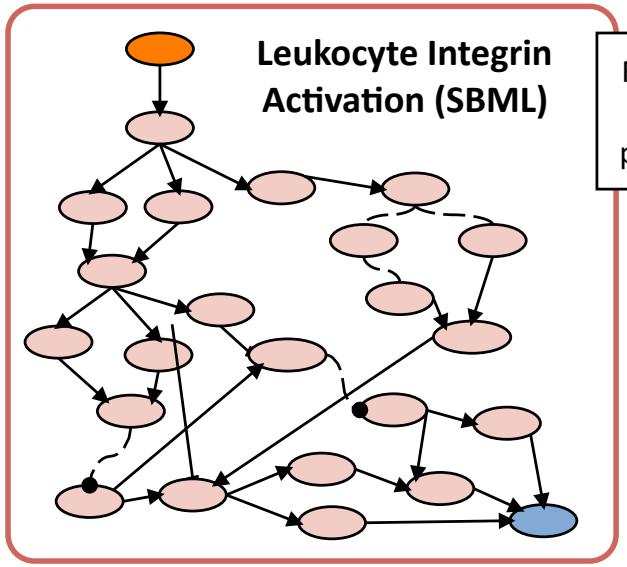


Modeling Overview

Model	Type	Feat.	Properties
Interaction graphs		• No time • No concentrations	Dependency matrix Source-target pathways Activators (strong/weak) Inhibitors (strong/weak) Feedback loops (pos, neg) Degree (scale free, etc.) Monotony Minimal intervention set (MIS)
Boolean models	Qualitative modeling	• Time (instants) • No concentrations	+ • Simple attractors – Steady/stable states • Complex attractors – Oscillations • Robustness & sensitivity
***Extended* Boolean models**	Semi-quantitative modeling	• Time (instants) • Concentrations (%)	+ • Accuracy…
Ordinary differential equations (ODEs)	Quantitative modeling	• Time (actual) • Concentrations (actual)	• Parametrization – Using experimental data

Example





IBM FoCs

Front-end parser

Checkers

Phase 1: Parametrization (ABV)

Signalling network SystemC model

Automatic test pattern generation

Testbenches (useful configurations)

Mutation model

Phase 2: Robustness/sensitivity analysis (ABV + Mutation analysis)

Signalling network SystemC model

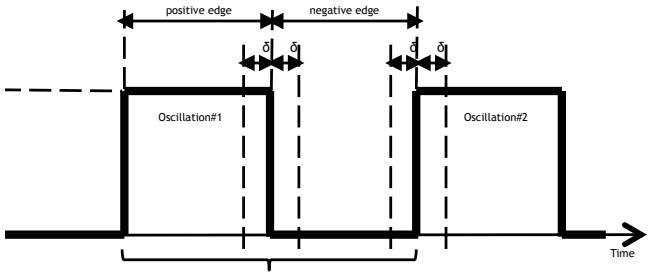
Checkers

Results

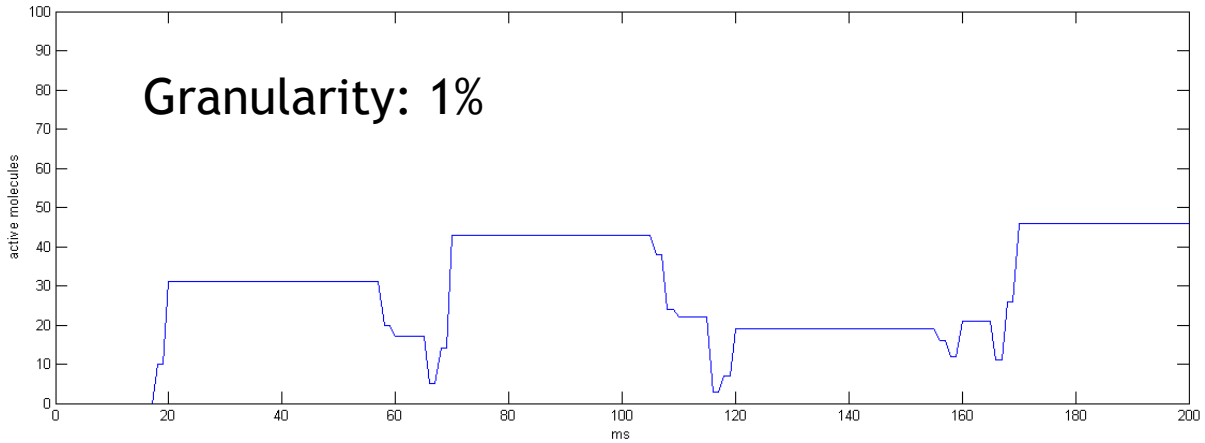
Qualitative modeling: results

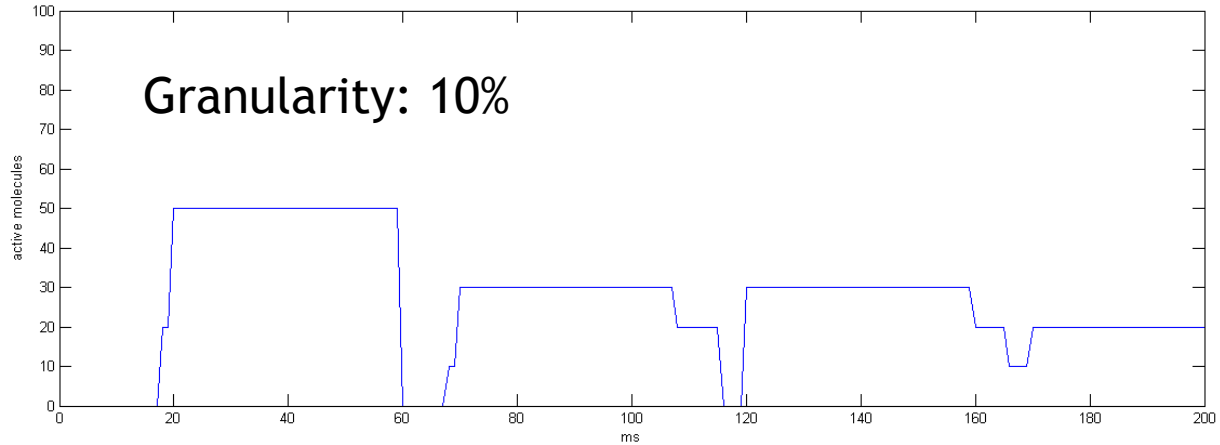
Mutated protein	Aperiodic config.	Useful conf. (periodic)	Oscill. (#)	Period ms
Golden model	-	2,008,188	2	50(±20%)
CXCR4	0	0	0	0
JAK3	2,008,188	0	2-4	-
JAK2	2,008,188	0	2-4	-
ABG	0	2,008,188	2	50(±20%)
VAV1	0	0	0	0
PLC	0	2,008,188	2	50(±20%)
RAC1	860,652	1,147,536	1-3	50(±20%)
RHOA	860,652	1,147,536	1-3	50(±20%)
CDC42	2,008,188	0	2-4	-
IP3	0	2,008,188	2	50(±20%)
DAG	17,640	1,990,548	1-2	50(±20%)
PLD1	0	0	0	0
PIP5K1C	0	0	0	0
CA	0	2,008,188	2	50(±20%)
RASGRP1	0	2,008,188	2	50(±20%)
PA	0	0	0	0
RAP1A	0	2,008,188	2	50(±20%)
PIP2	0	0	0	0
RIAM	0	2,008,188	2	50(±20%)
RASSF5	0	2,008,188	2	50(±20%)
TLN1	792,036	1,216,152	2-3	50(±20%)
FERMT3	952,140	1,056,048	2-4	50(±20%)

Parametrization over
≈ 2 x 10^9 configurations
Total simulation time:
≈ 4h



Semi-quantitative modeling: results

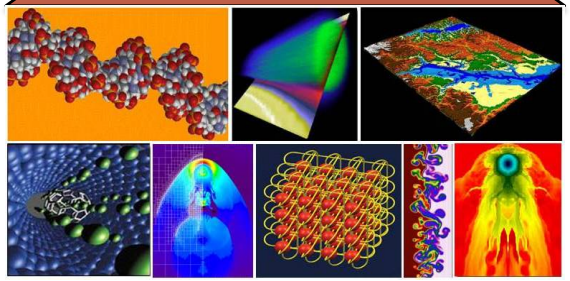


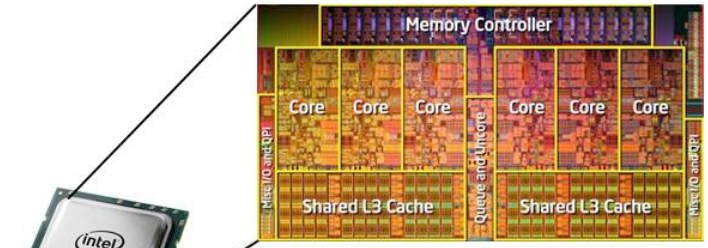


Parallel simulation

Parallelism and parallel architectures:

- **GPUs**
  - NVIDIA CUDA
    (Fermi, Kepler, Maxwell technology)
  - OpenCL/OpenACC
    (AMD APU technology)





- **Multi-core CPUs**
  - OpenMP

- **Cluster architectures:**
  - MPI