COPASI®: Introduction

Stefan Hoops

COPASI User Workshop

July 2014

www.copasi.org

Overview

- Biochemical Reaction Network
- Deterministic Simulation
- Stochastic Simulation
- COPASI Model
- Model Translation
- Steady State

Biological Process

What is a biological process?

Participants:
molecules, genes, proteins, complexes, drugs, etc.

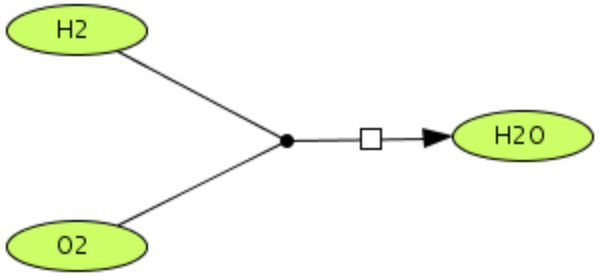
Participant Roles:
input, output , modifiers

Happens with a speed, propability, or frequency

Process Examples

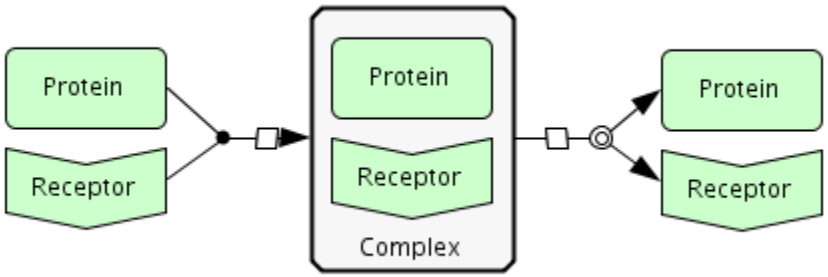
Chemical Reaction:

$2 * H_2 + O_2 \rightarrow 2 * H_2O$



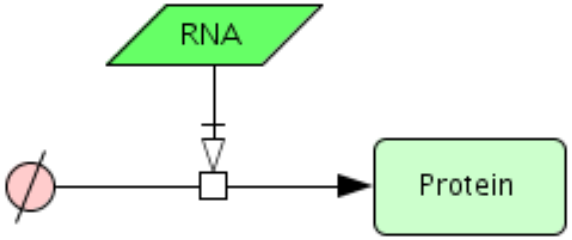
Complex Formation:

Protein A + Protein B = Complex



Process Examples

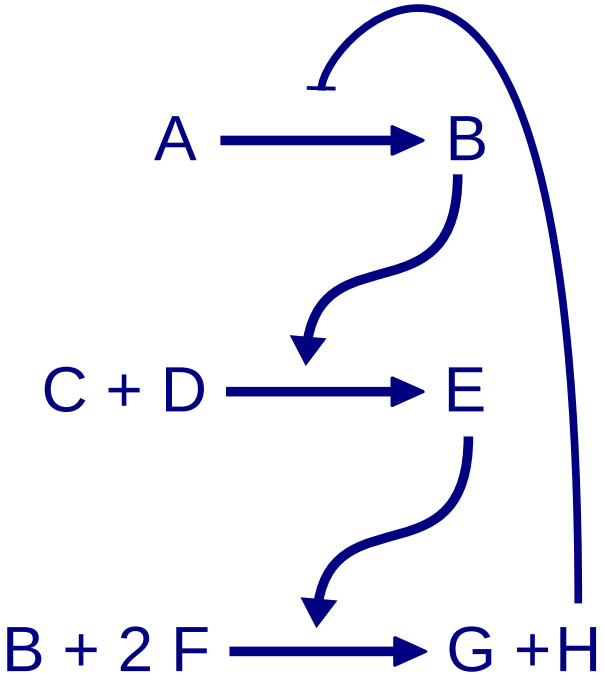
Translation:



-> Protein; RNA

Note: RNA is not consumed

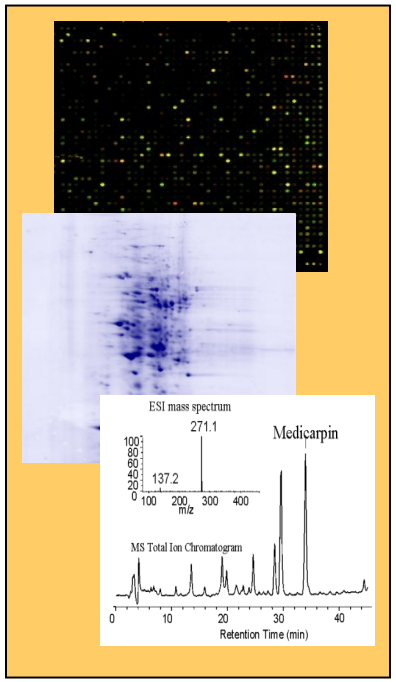
Biochemical Reaction Network



Genome

Proteome

Metabolome



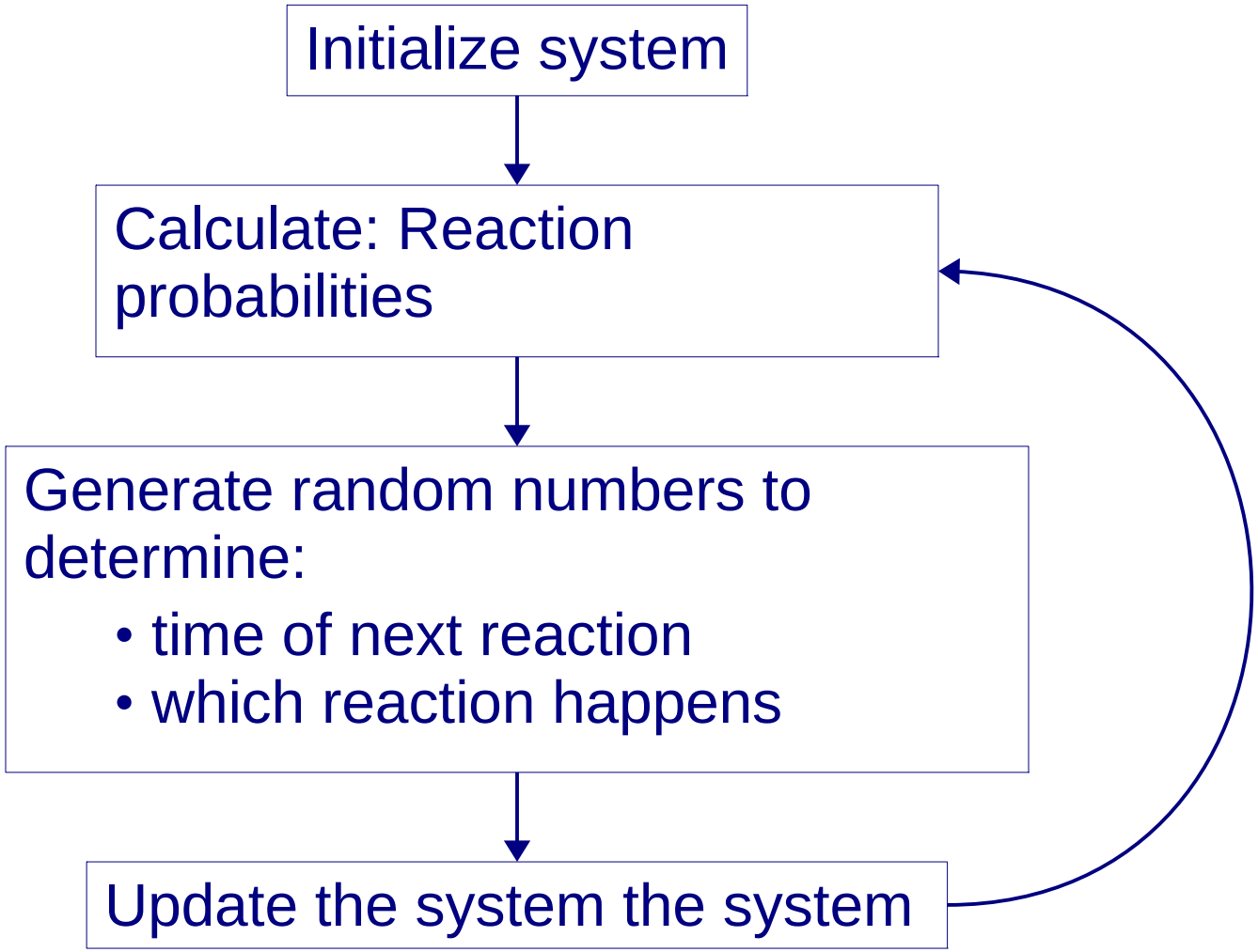
Deterministic Simulation

ODE System:

$$\begin{pmatrix} \dot{A} \\ \dot{B} \\ \dot{C} \\ \dot{D} \\ \dot{E} \\ \dot{F} \\ \dot{G} \\ \dot{H} \end{pmatrix} = \begin{pmatrix} -1 & 0 & 0 \\ 1 & 0 & -1 \\ 0 & -1 & 0 \\ 0 & -1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & -2 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} v_1(A, B, H) \\ v_2(B, C, D, E) \\ v_3(B, E, F, G, H) \end{pmatrix}$$

$\dot{x} = N\,v$ with: $\mathbf{x} = \begin{pmatrix} x_1 \\ x_2 \\ \dots \\ x_n \end{pmatrix}$ $\mathbf{v} = \begin{pmatrix} v_1 \\ v_2 \\ \dots \\ v_m \end{pmatrix}$

Stochastic Simulation



Stochastic Simulation

- Reactions are discrete events.
- Reaction events fire with a probability

$$P = k * S_1 * S_2 * \ldots$$

  depending on the reaction substrates S_i.

- Reactions are irreversible

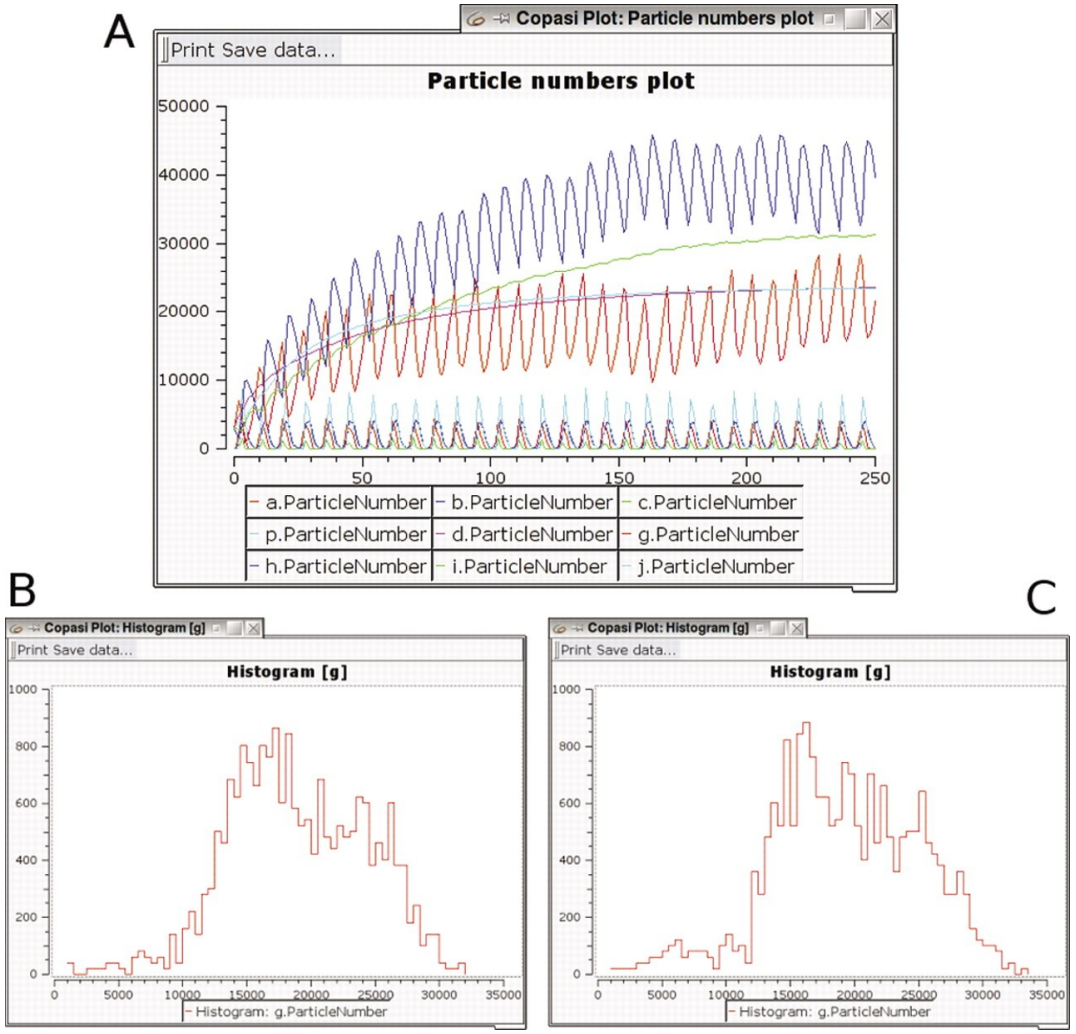
COPASI Model

- COPASI models are reaction networks.
- The tool “Convert to Irreversible” helps the user to convert each reversible reactions into 2 irreversible reactions.
- Kinetic laws may be interpreted as reaction velocities or as reaction probabilities through a user settable flag.

Hybrid Methods

- Switching between stochastic and deterministic integration depending on the smallest particle number (min(PN)) currently present in the model.
  - Start with stochastic simulation.
  - If (min(PN) < Lower Bound) switch to stochastic simulation.
  - If (min(PN) > Upper Bound) switch to deterministic simulation.

Hybrid Methods



Translating Kinetic Laws

$2\ A_2 + B_2 \rightarrow 2\ A_2B$ with Mass Action Kinetics

deterministic:

$$v = k\,[A_2]\,[A_2]\,[B_2]$$

stochastic:

$$p = k\,A_2\,(A_2 - 1)\,B_2$$

$2\ A_2 + B_2 \rightarrow 2\ A_2B$ with positive kinetics $f([A_2], [B_2])$

deterministic:

$$v = f([A_2], [B_2])$$

stochastic:

$$p = f([A_2], [B_2])\ \frac{A_2\,(A_2 - 1)\,B_2}{[A_2]\,[A_2]\,[B_2]}$$

Steady-State

Condition:

$$\dot{x} = N\,v = 0 \quad \text{with:} \quad \mathbf{x} = \begin{pmatrix} x_1 \\ x_2 \\ \dots \\ x_n \end{pmatrix} \quad \mathbf{v} = \begin{pmatrix} v_1 \\ v_2 \\ \dots \\ v_m \end{pmatrix}$$

Method:

- Damped Newton
- Forward Integration
- Backward Integration