

COPASI[®]: Introduction

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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:

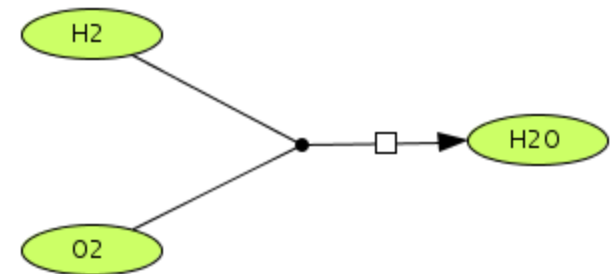
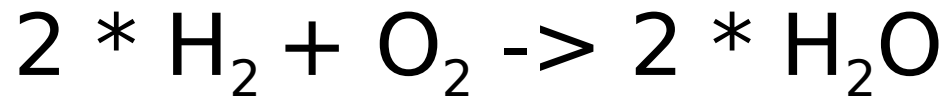
input, output , modifiers

Happens with a speed, propability, or
frequency



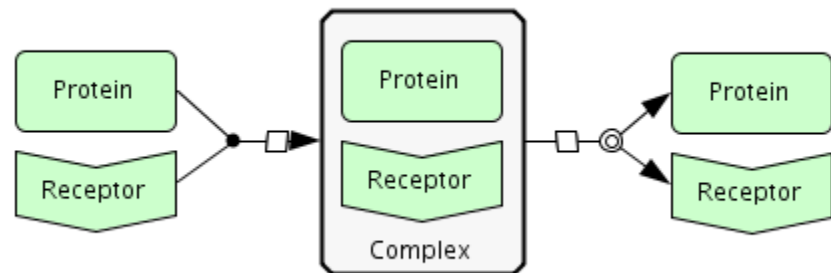
Process Examples

Chemical Reaction:



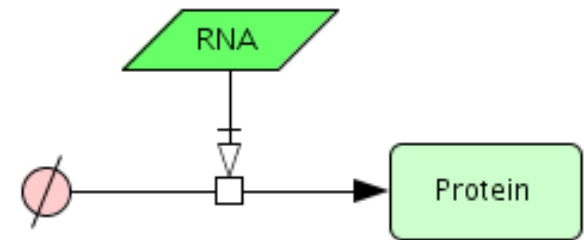
Complex Formation:

Protein A + Protein B = Complex



Process Examples

Translation:

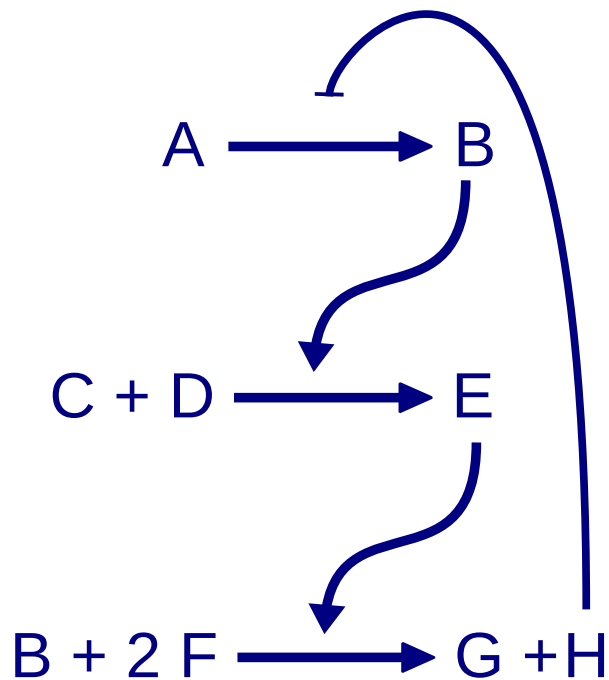


-> Protein; RNA

Note: RNA is not consumed



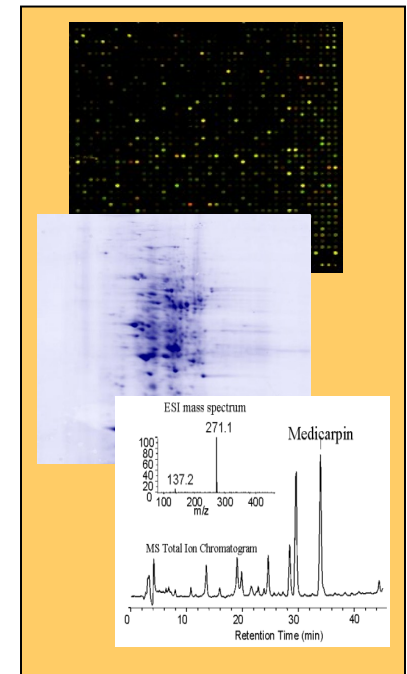
Biochemical Reaction Network



Genome

Proteome

Metabolome



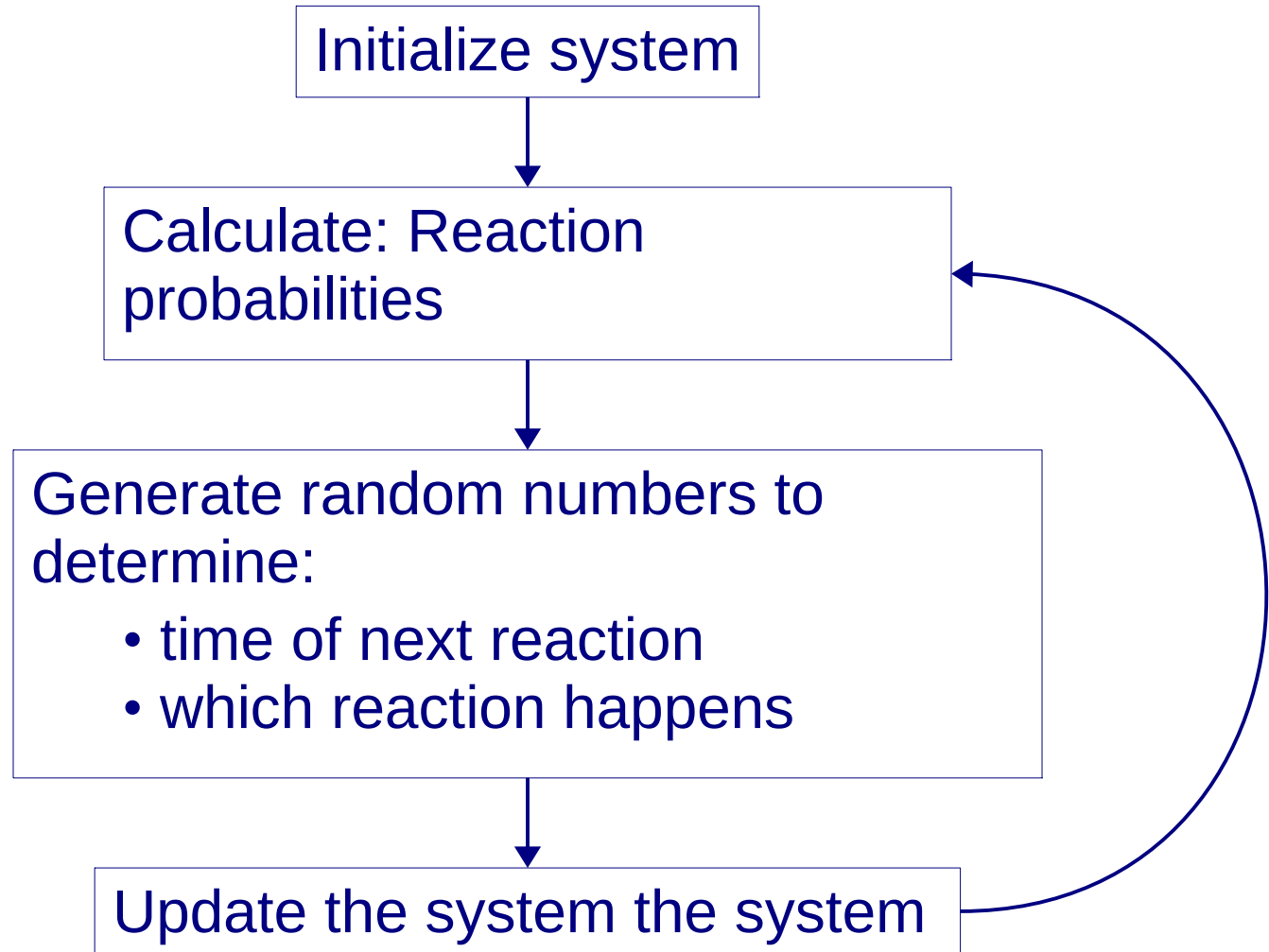
Deterministic Simulation

ODE System:

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

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

Stochastic Simulation



Stochastic Simulation

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

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

depending on the reaction substrates S_i .

- ▶ Reactions are irreversible

COPASI Model

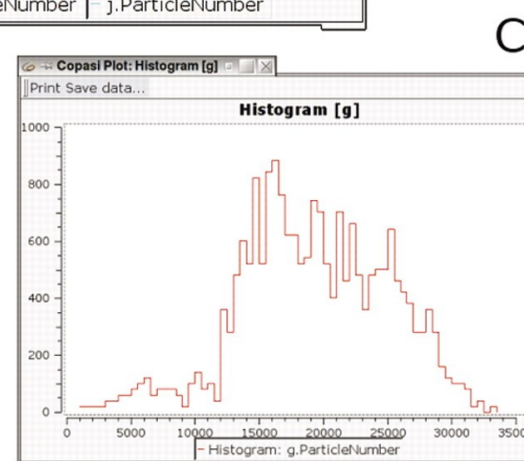
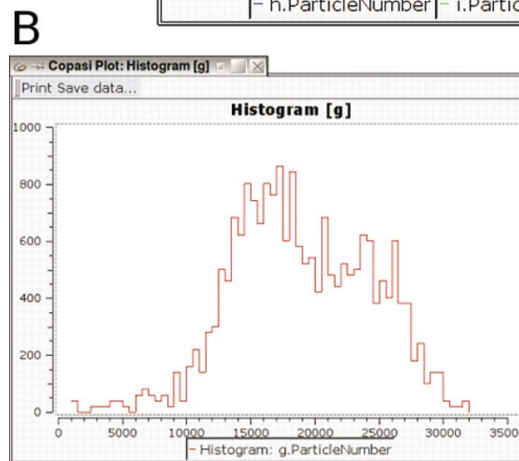
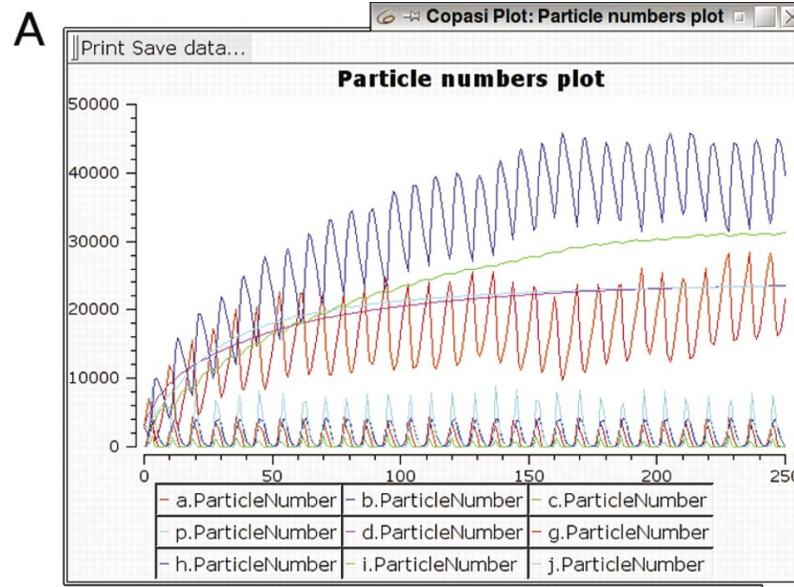
- ▶ COPASI models are reaction networks.
- ▶ The tool “Convert to Irreversible” helps the user to convert each reversible reactions into 2 irreversible reactions.
- ▶ Kinetic laws may be interpreted as reaction velocities or as reaction probabilities through a user settable flag.



Hybrid Methods

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

Hybrid Methods



Translating Kinetic Laws

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

deterministic:

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

stochastic:

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

$2 A_2 + B_2 \rightarrow 2 A_2 B$ 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:

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

Method:

Damped Newton
Forward Integration
Backward Integration