Models and Languages for Computational Systems Biology

Lecture 14: Continuous Petri Nets and Differential Equations

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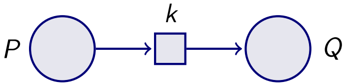
Monday 8 March 2010
Semester 2 Week 9

Simple Reaction



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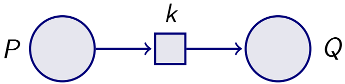

$$P \xrightarrow{k} Q$$

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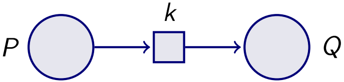

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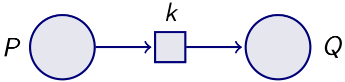

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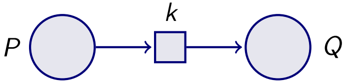

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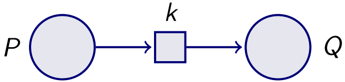

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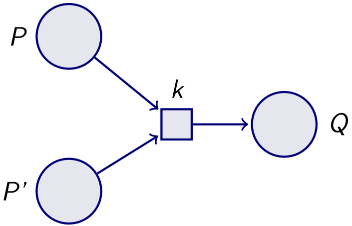

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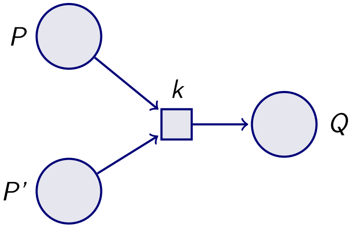

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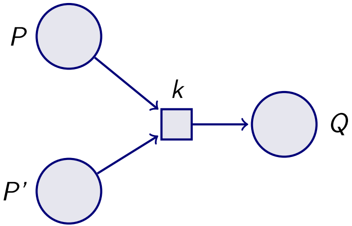

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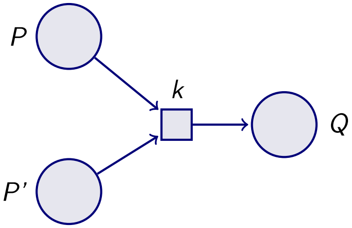

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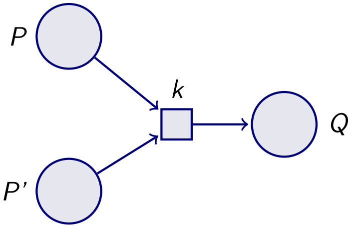

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$$[P']_t + [Q]_t = [P']_0 + [Q]_0$$

Continuous Petri Nets

A *continuous Petri net* is like a regular Petri net, but:

- Replaces token counts with real-valued quantities, representing *amount* or *concentration*;
- Adds a real-valued *reaction rate* or *flow rate* to each transition.

Here we assume mass-action kinetics: for more general kinetics, each transition may have an arbitrary *firing rate function* attached.

Different kinds of net

Discrete Petri net	Discrete event, untimed, discrete state space.
Stochastic Petri net	Discrete event, continuous time, discrete space.
Continuous Petri net	Continuous time, continuous state space.

Amounts and Concentrations

Moving between discrete models and continuous models may involve some work with unit conversion.

Number of molecules	x	
Amount of substance	x/N_A	mol
Avogadro number	$N_A \approx 6.022 \times 10^{23}$	mol^{-1}
Volume	V	l
Concentration	$c = \dfrac{x}{V \times N_A}$	$\mathrm{mol\,l^{-1}}$, M, μM, etc.

Rate of transition	$\mathrm{s^{-1}}$, $\mathrm{min^{-1}}$, etc.
Rate of change of amount	$\mathrm{mol\,s^{-1}}$, $\mathrm{mol\,min^{-1}}$
Rate of change of concentration	$\mathrm{mol\,l^{-1}\,s^{-1}}$, $\mathrm{M\,s^{-1}}$, $\mu\mathrm{M\,min^{-1}}$, etc.

Transition and Flow Rates

The correspondence between transition rate (firing rate, hazard rate) r of discrete events and flow rate (kinetic rate, reaction rate) k of a continuous reaction depends on the underlying stoichiometry.

Reaction	Kinetic rate	Units of k	Correspondence
$0 \rightarrow P$	k	$\mathsf{M\,s}^{-1}$	$r = N_A V k$
$P \rightarrow Q$	$k[P]$	s^{-1}	$r = k$
$P + P' \rightarrow Q$	$k[P][P']$	$\mathsf{M}^{-1}\,\mathsf{s}^{-1}$	$r = \dfrac{k}{N_A V}$
$P + P \rightarrow Q$	$k[P]^2$	$\mathsf{M}^{-1}\,\mathsf{s}^{-1}$	$r = \dfrac{2k}{N_A V}$

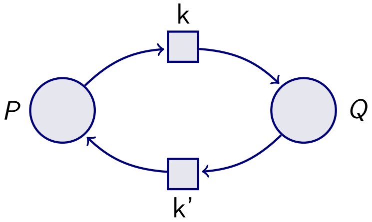
Scheme for Continuous Modelling

Continuous Petri nets give a graphical presentation for a collection of reaction formulae. From these we can derive in turn some or all of:

- Ordinary Differential Equations (ODE) known as the *reaction rate equations*;
- Exact analytic solutions for concentrations over time; (usually not)
- Approximate numerical solutions over time, for given initial conditions;
- Trajectories in *phase space*;
- Conservation laws;
- Points of equilibrium (may be stable, unstable, attractors or not).

In all of these the system behaviour is *deterministic*.

Example: Reversible Reaction



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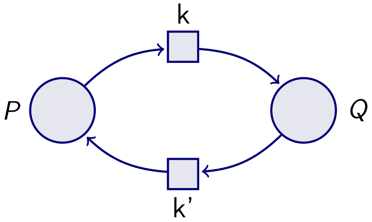

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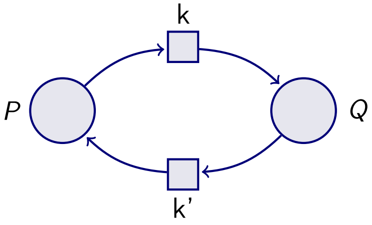

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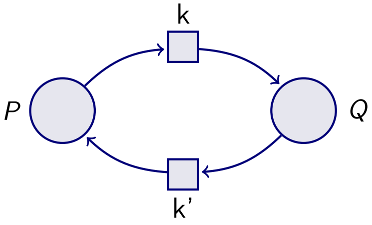

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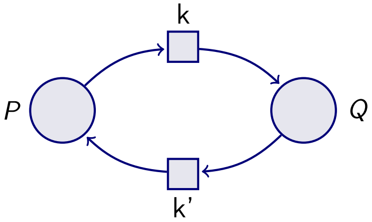

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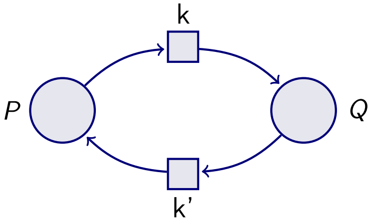

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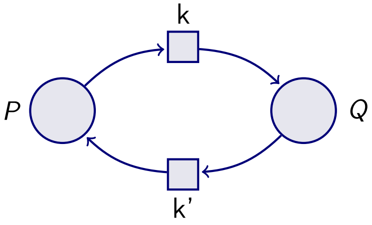

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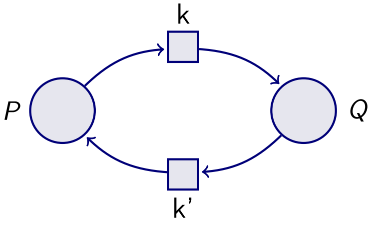

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$$[P]_t + [Q]_t = [P]_0 + [Q]_0$$

$$[P]_{eq} = \frac{k'}{k + k'}([P]_0 + [Q]_0)$$

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Further Examples

Example: Michaelis-Menten enzyme kinetics

Example: Lotka-Volterra dynamics

Review: Models of Many Kinds

Some possible modes of variation among mathematical models, logics, and other analyses for investigating the systems behaviour over time.

- Qualitative; Quantitative.
- Untimed; Timed.
- Discrete events; Continuous flow.
- Discrete state space; Continuous state space.
- Nondeterministic; Probabilistic/Stochastic; Deterministic.
- Linear-time; Branching-time.

Reading

Homework

Read §§6–9 of Heiner et al., about continuous Petri nets, and §§1–4 of Ciocchetta and Hillston, on BioPEPA.

M. Heiner, D. Gilbert, and R. Donaldson.
Petri Nets for systems and synthetic biology.
In *Formal Methods for Computational Systems Biology*, LNCS 5016, pp. 215–264. Springer-Verlag, 2008.

F. Ciocchetta and J. Hillston.
Bio-PEPA: A framework for the modelling and analysis of biochemical systems.
Theoretical Computer Science, 410(33–34):3065–3084, August 2009.