Global asymptotic stability of solutions of nonautonomous master equations

Extensions of van Kampen's Theorem

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satisfy the *Chapman-Kolmogorov equations*

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$$a_{ij} \text{ right-continuous}, \quad a_{ij} \geq 0 \ (i \neq j), \quad a_{jj} = -\Sigma_{i \neq j} a_{ij}$$

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one derives *master equation* from CKE in the limit $\Delta t \to 0$:

$$\frac{d\mathbf{p}_j}{dt} = A(t)\mathbf{p}_j$$

$$A(t) = (a_{ij}(t)), \quad \mathbf{p}_j = (p_{0j}, \dots, p_{nj})^T, \quad p_{ij}(t) = p(i, t|j, 0)$$

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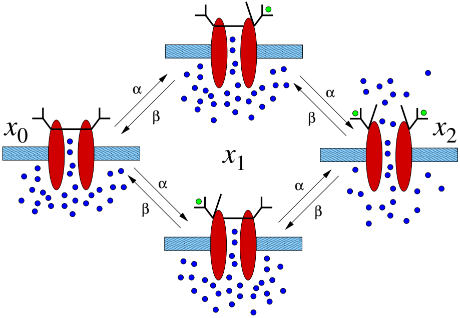
- Matrices like $A(t)$ called $\mathbb{W}$-matrices [van Kampen]

Ion channel with two identical, independent subunits



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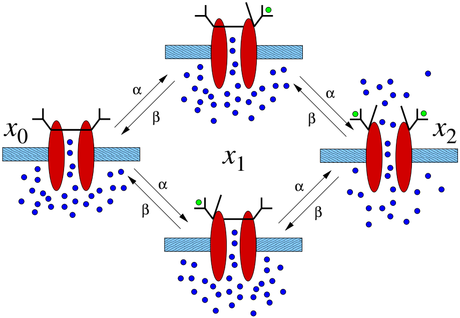

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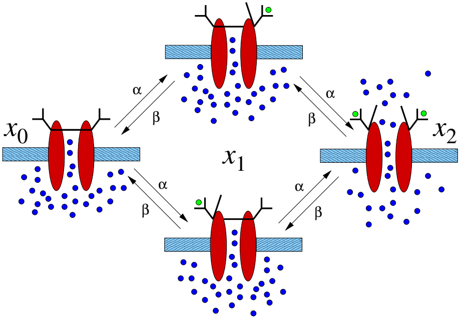

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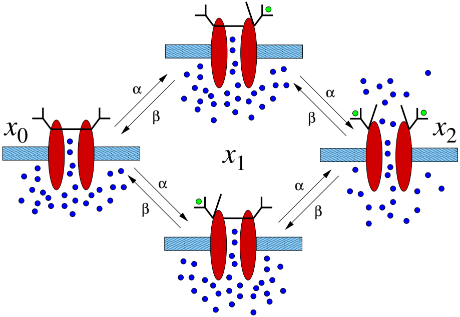

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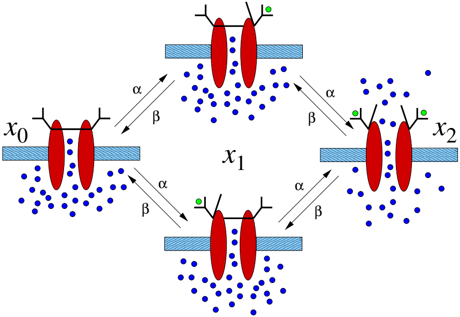

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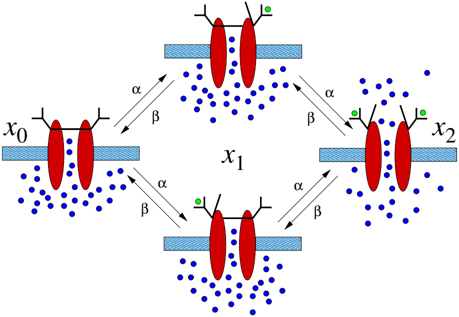
State diagram: $x_0 \underset{\beta}{\overset{2\alpha}{\rightleftarrows}} x_1 \underset{2\beta}{\overset{\alpha}{\rightleftarrows}} x_2$

Master equation for ion channel kinetics



$$x_0 \underset{\beta}{\overset{2\alpha}{\rightleftharpoons}} x_1 \underset{2\beta}{\overset{\alpha}{\rightleftharpoons}} x_2$$

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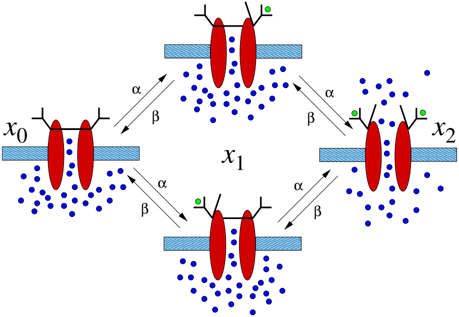

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Master equation: $$\frac{d\mathbf{p}}{dt} = A\mathbf{p} = \begin{bmatrix} -2\alpha & \beta & 0 \\ 2\alpha & -\alpha-\beta & 2\beta \\ 0 & \alpha & -2\beta \end{bmatrix} \begin{bmatrix} p_0 \\ p_1 \\ p_2 \end{bmatrix}$$

Behavior of solutions of autonomous master equation

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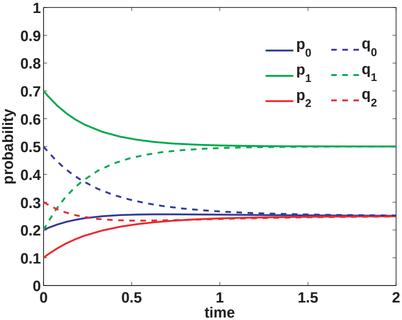
$\alpha = \beta = 1$



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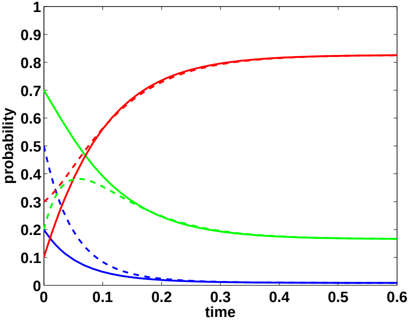

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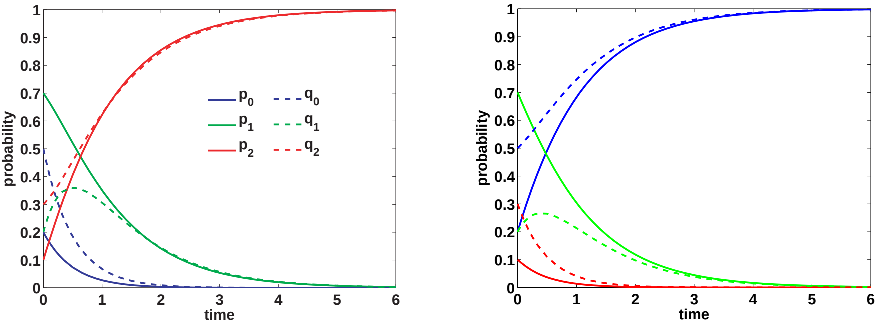
$\alpha = 1,\ \beta = 0$ $\qquad\qquad$ $\alpha = 0,\ \beta = 1$



van Kampen's theorem for autonomous master equations

Theorem

Suppose A is a constant $\mathbb{W}$-matrix. If A is neither decomposable nor splitting, then every probability distribution solution of the master equation approaches a unique stationary distribution.

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A is *decomposable* if there exists permutation matrix P such that

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- Zero is repeated eigenvalue $\Leftrightarrow$ decomposable or splitting

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where $\mathbf{v}_i$'s are eigenvectors and c_i's are polynomials in t

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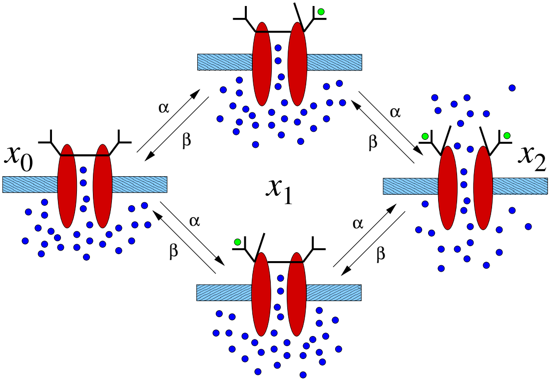
- Therefore, $\mathbf{p}(t) \to \mathbf{v}_0$ independent of initial conditions
- Note: converse of theorem is also true

Nonautonomous master equation



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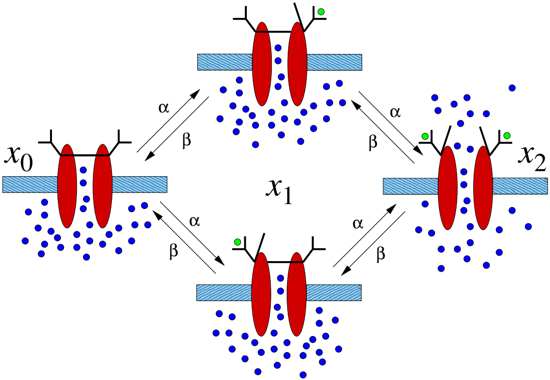

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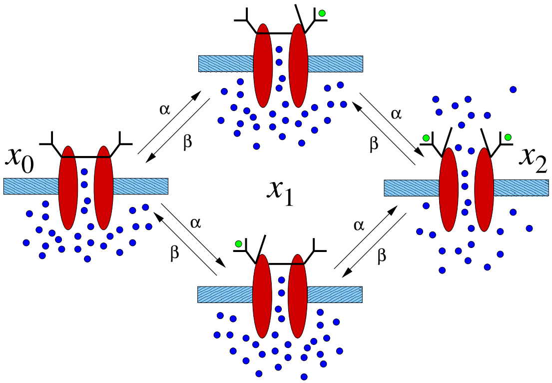

- Ion channel kinetics depend on *external* factors – e.g., membrane voltage and ligand concentration
- Open and close rates α, β are functions of time!
- How will solutions behave now?

Behavior of solutions of nonautonomous master equation

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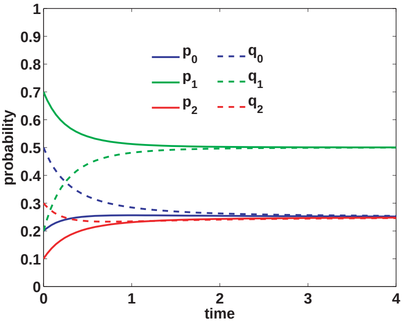
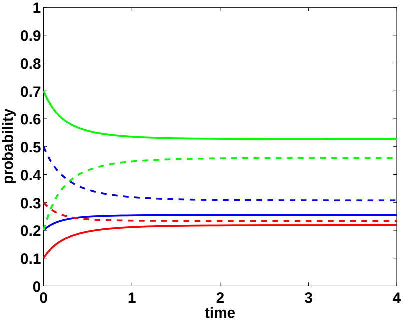
$\alpha = \beta = (t+1)^{-1}$



$\alpha = \beta = \exp(-2t)$



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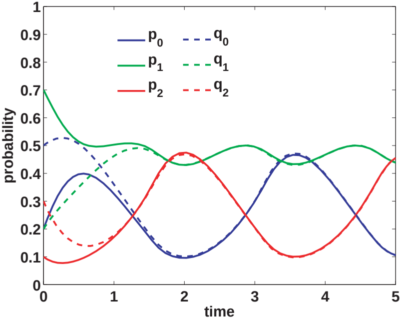
$\alpha = |\sin(t)|, \ \beta = |\cos(t)|$



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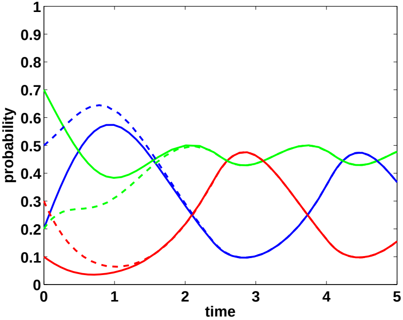

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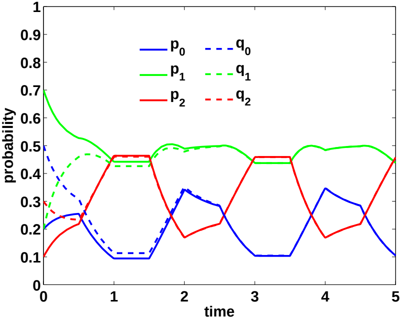
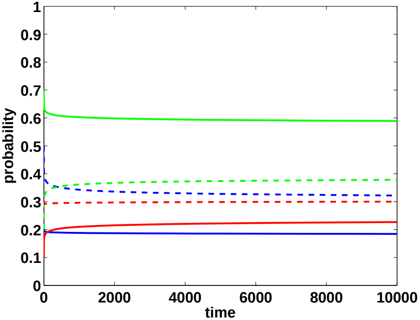
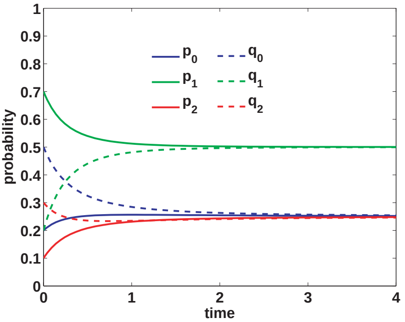


$$\alpha = \sin(2\tan^{-1}(100t)),$$
$$\beta = \cos(\tan^{-1}(100t))$$



First extension of van Kampen's theorem

$$\alpha(t) = \beta(t) = (t+1)^{-1}$$



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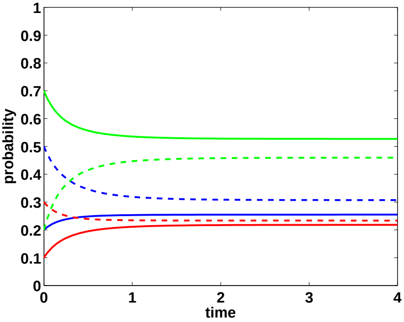

$$A(t) = \alpha(t) \begin{bmatrix} -2 & 1 & 0 \\ 2 & -2 & 2 \\ 0 & 1 & -2 \end{bmatrix}$$

First extension of van Kampen's theorem

Theorem

Suppose $A(t) = f(t)M$ *for all* $t \geq 0$*, where* M *is constant* $\mathbb{W}$*-matrix and* $f : \mathbb{R}_+ \to \mathbb{R}_+$ *is right-continuous. Then every probability distribution solutions of the master equation approaches a unique stationary distribution if and only if* M *is neither decomposable nor splitting and* f *is not integrable.*

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- Proof similar to van Kampen's theorem since FMS is

$$\Phi_0^t = \exp\left(\int_0^t A(t)\right) = \exp\left(F(t)M\right) \quad \left(F(t) = \int_0^t f(s)\,ds\right)$$

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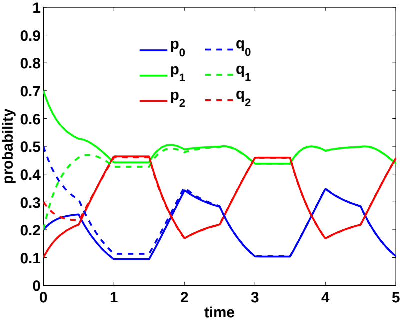
where $\mu_i, \mathbf{v}_i$ are eigenpairs of M and c_i's are polynomials in $F(t)$

- $\mathbf{p}(t) \to \mathbf{v}_0 \Leftrightarrow \Re(\mu_i) < 0$ for $i = 1, \ldots, n$, and $F(t) \to \infty$

Extension for asymptotically periodic A

$\alpha = \Theta(\sin(\pi t))$, $\beta = \Theta(\cos(\pi t))$



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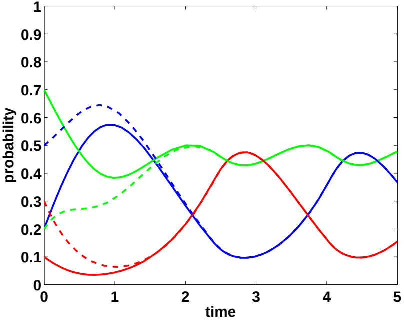

- In both cases, A approaches a periodic matrix

Extension for asymptotically periodic A

Definition

The probability distribution solutions of a master equation are *globally asymptotically stable* (GAS) if for every pair of such solutions $\mathbf{p}, \mathbf{q}$

$$\mathbf{p}(t) - \mathbf{q}(t) \to \mathbf{0} \text{ as } t \to \infty.$$

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Theorem

Suppose A is a right-continuous, $\mathbb{W}$-matrix-valued function, and that there exists a continuous, periodic, $\mathbb{W}$-matrix-valued function B, whose ω-limit set contains at least one matrix that is neither decomposable nor splitting, such that

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Then the probability distribution solutions of the master equation are GAS.

- Proof: For large t, $\mathcal{L}^1$-norm of $\mathbf{p} - \mathbf{q}$ must decrease by some uniform, nonzero amount during each period of B.

Another extension of van Kampen's theorem

Theorem

If A is differentiable, $\mathbb{W}$-matrix-valued function such that both A and its derivative are bounded, and the ω-limit set of A contains no matrix which is either decomposable or splitting, then probability distribution solutions of the master equation are GAS.

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- Proof: if $||\mathbf{p}(t) - \mathbf{q}(t)||_1 \to r > 0$, then $\omega(A)$ contains a decomposable or splitting matrix

One might conjecture...

- Let $\lambda_0, \lambda_1, \ldots, \lambda_n$ be an ordering of the eigenvalues of A such that

$$0 = \lambda_0(t) \geq \Re(\lambda_1(t)) \geq \cdots \geq \Re(\lambda_n(t))$$

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- In each extension, the eigenvalues $\lambda_1, \ldots, \lambda_n$ are not integrable
  - Scalar time-dependence: $\lambda_1(t) = f(t)\mu_1$
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- The nonintegrability of $\Re(\lambda_1)$ "should" ensure that $||\mathbf{p}(t) - \mathbf{q}(t)||_1 \to 0$

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$$A(t) = \frac{1-\cos(\pi t)}{2} A_1(t) + \frac{1-\cos(\pi(t+1))}{2} A_2(t)$$

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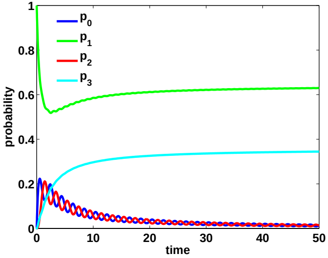

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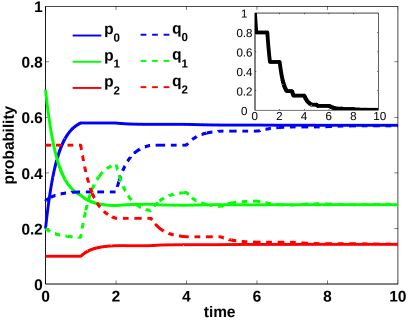

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Conjecture

If the derivative of A is bounded and the ω-limit set of contains at least one matrix which is neither decomposable nor splitting, then the probability distribution solutions of the master equation are GAS.

Thank you!

Thanks to

- Jim Keener (Utah)
- NSF