

Markovian-modulated Models and Their Application Potential

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Example 1: Microsatellite

The components of the model¹:

- 1 Two-dimensional state space

$$S = \{(n, m) : n = 0, 1, 2, \dots; m = 0, 1, \dots, n\} \quad (1)$$

consisting of

- n - the number of repeat units
- m - the number of those which are impure

- 2 Appropriately chosen generator

$$\mathbf{Q} = [q_{(i,j)(k,\ell)}] \quad (2)$$

(slipped-strand mispairing, point mutation)

¹T. Stark, B. McCormish, M. O'Reilly, B. Holland. A purity dependent Markov model for the time-evolution of microsatellites. *In preparation*.

Example 2: Gene family

The components of the model²:

- 1 Two-dimensional state space

$$S = \{(n, m) : n = 0, 1, 2, \dots; m = 0, 1, \dots, n\} \quad (3)$$

consisting of

- n - the number of copies
- m - the number of those which are redundant

- 2 Appropriately chosen *time-inhomogenous* generator

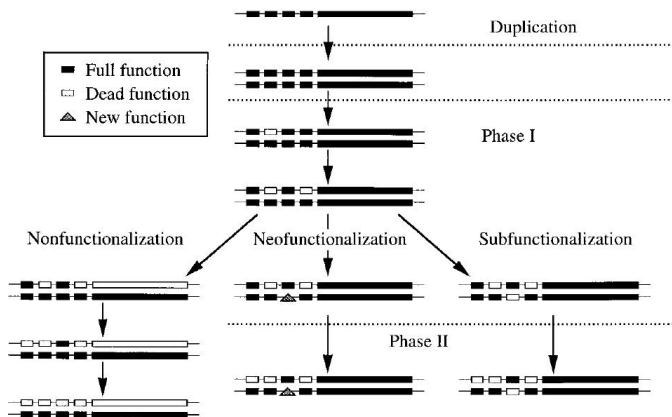
$$\mathbf{Q}(t) = [q_{(i,j)(k,\ell)}(t)] \quad (4)$$

(duplication, loss, neofunctionalization,
 subfunctionalization)

²A.I. Teufel, J. Zhao, M. O'Reilly, L. Liu, D. A. Liberles. On mechanistic modeling of gene content evolution: Birth-Death models and mechanisms of gene birth and gene retention. *Computation*, 2:112–130, 2014.

Neofunctionalization/Subfunctionalization

Figure 1 in³



³ A. Force, M. Lynch, F.B. Pickett, A. Amores, Y. Yan, J. Postlethwait. Preservation of Duplicate Genes by Complementarity, Degenerative Mutations. *Genetics* 151:1531–1545, 1999.

Modeling assumptions

- duplication rate $c > 0$ per copy of a gene
- loss rate $a > 0$ per redundant copy of a gene
- loss rate $b > 0$ per non-redundant copy of a gene
- neofunctionalization rate $g > 0$ per copy of a gene
- subfunctionalization rate $h(t)$ per copy of a gene, where t is the time elapsed since the last state transition, given by the density of a gamma distribution

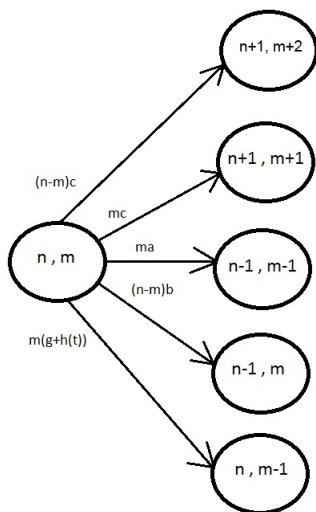
$$h(t) = \frac{(\beta t)^{\alpha-1} t e^{-\beta t}}{\Gamma(\alpha)} \quad \text{for } t \geq 0 \quad (5)$$

(α - shape parameter, β - rate parameter)

where

$$\Gamma(\alpha) = \int_{x=0}^{\infty} x^{\alpha-1} e^{-x} dx$$

Diagram of transitions out of (n, m)



Application and Numerical work

In preparation.⁴

⁴T. Stark, B. Holland, D. Liberles, M. O'Reilly

Continuous-time Markov Chain (CTMC)

CTMCs are used to model the *evolution of environments*.

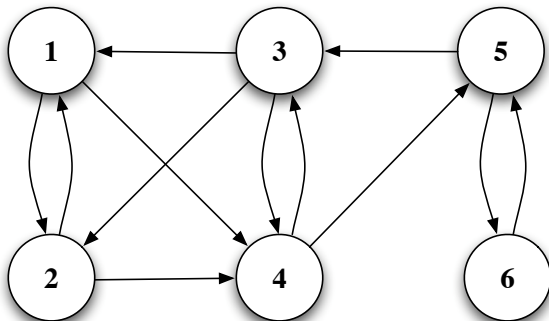
Key parameters:

- the set S of all possible phases
- generator matrix $\mathbf{T} = [T_{ij}]$ of transition rates.

Standard measures:

- $\mathbf{P}(t) = [P(t)_{ij}]$ records the probabilities of observing phase j at time t , given start in phase i
- $\boldsymbol{\pi} = [\pi]$ records the stationary probabilities of observing phase j .

Example - Hydro-Power Generation System



1 on-design, 2 off-design, 3 start, 4 stop, 5 idle, 6 maintenance

Standard Properties

Fact

$\mathbf{P}(t)$ is given by

$$\mathbf{P}(t) = e^{\mathbf{T}t}$$

Fact

π , whenever it exists, is the unique solution of

$$\begin{cases} \pi \mathbf{P} & = & \pi \\ \pi \mathbf{1} & = & 1 \end{cases}$$

Standard Techniques

- Embedded Chain - discrete-time Markov Chain (DTMC) with the same \mathcal{S} and matrix $\mathbf{P} = [p_{ij}]$ of jump probabilities given by

$$p_{ij} = \frac{T_{ij}}{-T_{ii}}$$

- Uniformized Chain - DTMC with the same \mathcal{S} and matrix

$$\mathbf{P}^* = \mathbf{I} + \frac{1}{\vartheta} \mathbf{T},$$

where

$$\vartheta \geq \max_i \{-T_{ii}\}$$

Simulating a CTMC

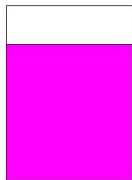
Two common methods:

- 1 a Generate the interarrival time τ_i given current time t and $X(t) = i$, from $Exp(\lambda_i)$ with $\lambda_i = -T_{ii}$.
b At time $t + \tau_i$ the process jumps to some state j with probability $p_{ij} = T_{ij}/\lambda_i$.

- 2 a Generate t_k from $Exp(T_{ik})$ for all $k \neq i, k \in S$.
b Let $\tau_i = \min_k \{T_{ik}\}$ and k^* be the corresponding value of k .
c The process jumps to state k^* at time $t + \tau_i$.

1-D Stochastic Fluid Model (SFM)

Model⁵: Two-dimensional state space $(X(t), \varphi(t))$ with level $X(t)$, phase $\varphi(t) \in \mathcal{S}$, generator \mathbf{T} , rates r_i

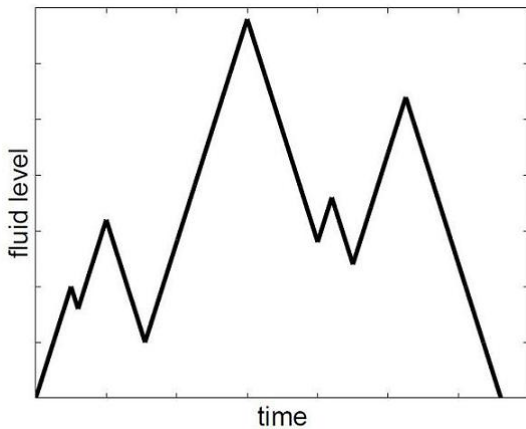


Buffer Y

$$\frac{dY(t)}{dt} = r_i \quad \text{when } \varphi(t) = i \text{ and } Y(t) > 0$$

⁵Bean, N. G., O'Reilly, M. M. and Taylor, P. G. (2005). Hitting probabilities and hitting times for stochastic fluid flows. *Stochastic Processes and Their Applications*, 115, 1530–1556.

Sample Path Example



Application example - Coral Bleaching



Results

Theoretical and numerical results for topics such as e.g.

- Return to the original level
- Draining/Filling to some level
- Avoiding some taboo level
- Unbounded, bounded and multi-layer buffers
- Various transient/stationary measures of interest

Uniformization of the 1-D SFM

Uniformization⁶ produces a (level-homogenous) Quasi-Birth-and-Death Process (QBD), a type of a CTMC with two-dimensional state space (level n , phase k)

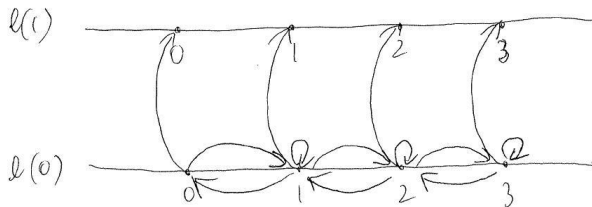
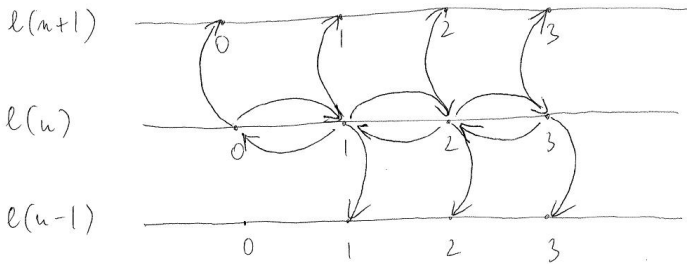
$$S = \{(n, k) : n = 0, 1, 2, \dots; k = 0, 1, \dots, m\} \quad (6)$$

and generator such that the visits to the neighbouring levels only are allowed,

$$\mathbf{Q} = \begin{array}{c|ccccc}
 & \ell(0) & \ell(1) & \ell(2) & \ell(3) & \dots \\
 \hline
 \ell(0) & \mathbf{B} & \mathbf{A}_0 & \mathbf{0} & \mathbf{0} & \dots \\
 \ell(1) & \mathbf{A}_2 & \mathbf{A}_1 & \mathbf{A}_0 & \mathbf{0} & \dots \\
 \ell(2) & \mathbf{0} & \mathbf{A}_2 & \mathbf{A}_1 & \mathbf{A}_0 & \dots \\
 \ell(3) & \mathbf{0} & \mathbf{0} & \mathbf{A}_2 & \mathbf{A}_1 & \dots \\
 \dots & \dots & \dots & \dots & \dots & \dots
 \end{array}$$

⁶4. N.G. Bean and M.M. O'Reilly. (2013) Spatially-coherent Uniformization of a Stochastic Fluid Model to a Quasi-Birth-and-Death Process. Performance Evaluation, 70(9): 578-592

Example: QBD transitions



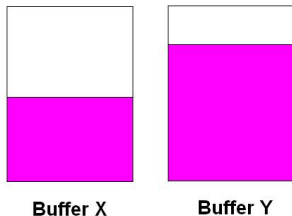
Uniformization of the 1-D SFM

The two examples at the start of this talk were QBDs!

$$\mathbf{Q} = \begin{array}{c} \ell(0) \\ \ell(1) \\ \ell(2) \\ \ell(3) \\ \dots \end{array} \left| \begin{array}{ccccc} \ell(0) & \ell(1) & \ell(2) & \ell(3) & \dots \\ \mathbf{B} & \mathbf{A}_0^{(0)} & \mathbf{0} & \mathbf{0} & \dots \\ \mathbf{A}_2^{(1)} & \mathbf{A}_1^{(1)} & \mathbf{A}_0^{(1)} & \mathbf{0} & \dots \\ \mathbf{0} & \mathbf{A}_2^{(2)} & \mathbf{A}_1^{(2)} & \mathbf{A}_0^{(2)} & \dots \\ \mathbf{0} & \mathbf{0} & \mathbf{A}_2^{(3)} & \mathbf{A}_1^{(3)} & \dots \\ \dots & \dots & \dots & \dots & \dots \end{array} \right|$$

2-D Stochastic Fluid Model

Model with two levels⁷

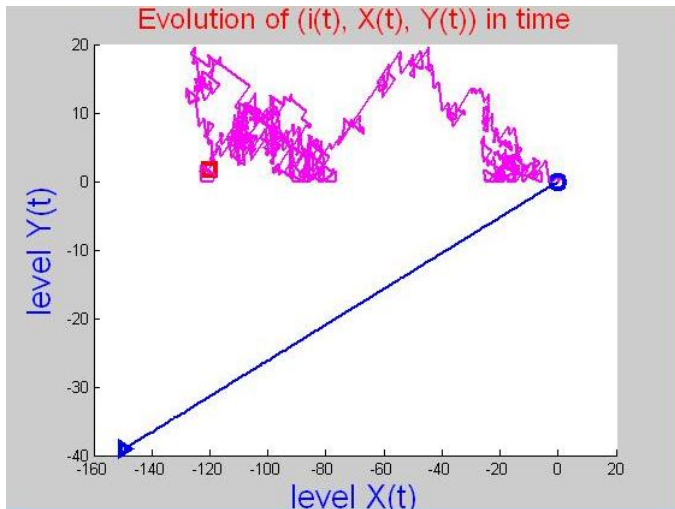


$$\frac{dX(t)}{dt} = c_i \quad \text{when } \varphi(t) = i$$

$$\frac{dY(t)}{dt} = r_i \quad \text{when } \varphi(t) = i \text{ and } Y(t) > 0$$

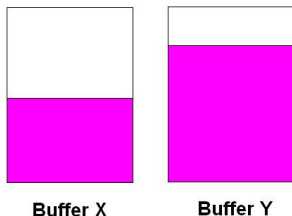
⁷5. N.G. Bean and M.M. O'Reilly. (2013) Stochastic Two-Dimensional Fluid Model. Stochastic Models, 29(1): 31-63.

Sample Path Example



Stochastic Fluid-Fluid Model

Model with two interacting levels⁸



$$\frac{dX(t)}{dt} = c_i \quad \text{when } \varphi(t) = i$$

$$\frac{dY(t)}{dt} = r_i(x) \quad \text{when } \varphi(t) = i, X(t) = x \text{ and } Y(t) > 0$$

⁸.G. Bean and M.M. O'Reilly. (2014) The stochastic fluid-fluid model: A stochastic fluid model driven by an uncountable-state process, which is a stochastic fluid model itself. Stochastic Processes and their Applications 124 (5): 1741-1772

Results for the 2-D SFMs

- Theoretical framework
- Numerical solutions

Current work:

- Time-dependent (cyclic) 1-D SFMs

Summary

Features of various Markovian-modulated models:

- discrete-time/continuous-time
- two-dimensional state space
- discrete phase variable
- discrete/continuous level variable
- level-varying parameters
- two, possibly interacting, level variables

Applications:

- Aanalysis of systems that evolve in time

Thanks!

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