Fluid and Mean Field Approximation: Moment closures and central limit approximation

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IMT, Lucca, September 30 - October 4, 2013

Outline

OVERVIEW

We will look at the relationship between the fluid equation and a Markov population model from the point of view of the average of the stochastic process.

- We will start from an heuristic argument.
- We then look at it more carefully and show a method to get ODE for the moments (mean, variance, and so on) of the process.
- Next, we will take the point of view of perturbation theory, Taylor-expanding the Kolmogorov equation around the mean (Kramers-Moyal expansion).
- Finally, we will look at another kind of expansion, the linear noise, that will bring us to the central limit theorem (Gaussian Process approximation).

Outline

1. Fluid Equation and Moments
2. System-Size Expansion
3. Linear Noise Approximation

AVERAGE OF CTMC MODEL

ODE FOR THE AVERAGE

Sometimes we are interested only in the (transient) average behaviour of the CTMC.
From Kolmogorov equations, we can derive an ODE for the average state $\mathbb{E}_t[\mathbf{X}]$ of the CTMC:

$$\frac{d\mathbb{E}_t[\mathbf{X}]}{dt} = \mathbb{E}_t[F(\mathbf{X})] = \sum_{\tau \in \mathcal{T}} \mathbf{v}_\tau \mathbb{E}_t[f_\tau(\mathbf{X})].$$

APPROXIMATIONS

If it holds that $\mathbb{E}_t[F(\mathbf{X})] = F(\mathbb{E}_t[\mathbf{X}])$, i.e. $\mathbb{E}_t[f_\tau(\mathbf{X})] = f_\tau(\mathbb{E}_t[\mathbf{X}])$ for all τ, then the previous equation boils down to the fluid ODE.
But this can be done exactly only if $F(\mathbf{X})$ is a linear function.
Otherwise, one can resort to an approximation of the ODE for the true average.

ODE FOR THE AVERAGE

SIMPLE SHARED RESOURCE MODEL

$$\frac{d\mathbb{E}_t[X_{P1}]}{dt} = k_2\mathbb{E}_t[X_{P2}] - \mathbb{E}_t[\min\{k_1 X_{P1}, h_1 X_{R1}\}]$$

$$\frac{d\mathbb{E}_t[X_{P1}]}{dt} \approx k_2\mathbb{E}_t[X_{P2}] - \min\{k_1\mathbb{E}_t[X_{P1}], h_1\mathbb{E}_t[X_{R1}]\}$$

SYNCHRONIZATION BY RATE PRODUCT

$$\frac{d\mathbb{E}_t[X_{P1}]}{dt} = k_2\mathbb{E}_t[X_{P2}] - k_1 h_1\mathbb{E}_t[X_{P1}X_{R1}].$$

$$\frac{d\mathbb{E}_t[X_{P1}]}{dt} \approx k_2\mathbb{E}_t[X_{P2}] - k_1 h_1\mathbb{E}_t[X_{P1}]\mathbb{E}_t[X_{R1}].$$

In this case, the equation for the true average depends on higher order moments.

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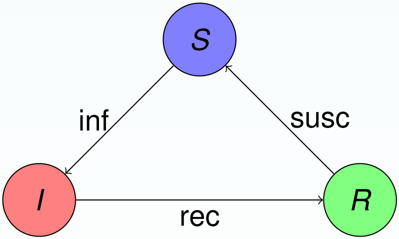
EXAMPLE: SIR EPIDEMICS



We obtain the same equation of the fluid approximation!

$$\begin{cases} \frac{d\mathbb{E}[X_S]}{dt} = k_S\mathbb{E}[X_R] - k_I\mathbb{E}[X_I]\mathbb{E}[X_S] \\ \frac{d\mathbb{E}[X_I]}{dt} = k_I\mathbb{E}[X_I]\mathbb{E}[X_S] - k_R\mathbb{E}[X_I] \\ \frac{d\mathbb{E}[X_R]}{dt} = k_R\mathbb{E}[X_I] - k_S\mathbb{E}[X_R] \end{cases}$$

MOMENT CLOSURE

DINKIN'S FORMULA FOR NON-CENTRED MOMENTS

$$\frac{d\mathbb{E}_t[X_1^{m_1}\cdots X_n^{m_n}]}{dt} = \sum_{\tau\in\mathcal{T}} \mathbb{E}_t\left[f_\tau(\mathbf{X})\left(\prod_{j=1}^{n}(X_j+\mathbf{v}_{\tau,j})^{m_j} - X_1^{m_1}\cdots X_n^{m_n}\right)\right].$$

SIR MODEL EXAMPLE

$$\begin{aligned}\frac{d\mathbb{E}_t[X_S^2]}{dt} &= \mathbb{E}_t[k_I/N\cdot X_S X_I((X_S-1)^2-X_S^2)] + \mathbb{E}_t[k_S\cdot X_R((X_S+1)^2-X_S^2)]\\ &= k_I/N\mathbb{E}_t[X_S X_I] - 2k_I/N\mathbb{E}_t[X_S^2 X_I] + 2k_S\mathbb{E}_t[X_S X_R] + k_S\mathbb{E}_t[X_R]\end{aligned}$$

The equation for the variance of X_S depends on third order moments.

For the SIR model, the equation for a moment of order N depend on moments of order $k+1$, due to quadratic non-linearity.

If we have polynomial rates of maximum degree m, then moments of order N depend on moments of order $k+m-1$.

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If rate functions f_τ are polynomial the previous equation depends only on non-centred moments. However, equations for moments of order k generally depend on moments of higher order: the system of ODE is not closed (infinite dimensional).
For smooth rate functions, one can approximate the rate with a Taylor polynomial.

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CLOSING THE EQUATIONS

Equations can be closed by replacing higher order moment with non-linear functions of lower order moments.
One example is normal moment closure (assume that moments from third on satisfy relation of a normal distribution).
Another example is log-normal moment closure.

NORMAL MOMENT CLOSURE

MOMENTS OF MULTIVARIATE NORMAL DISTRIBUTION

The central moments have a relatively simple form. The k-th centred moment, $k \geq 3$, is:

- zero, if k odd.
- Let $i_1, \ldots, i_k$ be indices in $\{1, \ldots, n\}$, non necessarily distinct, and let $\mathcal{L}$ be an allocation of $i_1, \ldots, i_k$ into $k/2$ unordered pairs. Then

$$\mathbb{E}[(X_{i_1} - \mu_{i_1}) \cdots (X_{i_k} - \mu_{i_k})] = \sum_{\mathcal{L}} \prod_{(j,h) \in \mathcal{L}} COV(X_{i_j}, X_{i_h})$$

Example: $\mathbb{E}[(X_1 - \mu_1)^2 (X_2 - \mu_2)(X_3 - \mu_3)] = VAR(X_1, X_1) COV(X_2, X_3) + 2COV(X_1, X_2) COV(X_1, X_3)$.

To close the equation for the second order moment of X_S, we can expand the definition of the third centred moment and use $\mathbb{E}[X_S^2 X_I] = 2\mathbb{E}[X_S]\mathbb{E}[X_S X_I] + \mathbb{E}[X_S^2]\mathbb{E}[X_I] - 2\mathbb{E}[X_S]^2 \mathbb{E}[X_I]$.

Outline

POPULATION CTMC: DEFINITIONS

MASTER EQUATION

$$\frac{dP(\mathbf{x},t)}{dt} = \sum_{\eta\in\mathcal{T}} r_\eta(\mathbf{x}-\mathbf{v}_\eta)P(\mathbf{x}-\mathbf{v}_\eta,t) - \sum_{\eta\in\mathcal{T}} r_\eta(\mathbf{x})P(\mathbf{x},t)$$

DRIFT

$$F(\mathbf{x}) = \sum_{\eta\in\mathcal{T}} \mathbf{v}_\eta r_\eta(\mathbf{x})$$

DIFFUSION MATRIX

$$D_{ik}(\mathbf{x}) = \sum_{\eta\in\mathcal{T}} \mathbf{v}_\eta[i]\mathbf{v}_\eta[k] r_\eta(\mathbf{x})$$

First-order approximation

Differential Equation for the Average of a PCTMC

$$\frac{d\mathbb{E}\left[X_i\right]_t}{dt} = \mathbb{E}\left[F_i(\mathbf{X})\right]_t$$

Taylor expansion of $\mathbb{E}\left[F_i(\mathbf{X})\right]_t$

$$\mathbb{E}\left[F_i(\mathbf{X})\right]_t \approx F_i(\mathbb{E}\left[\mathbf{X}\right]_t) + \frac{1}{2}\sum_{h,k=1}^{|\mathbf{Y}|} \partial^2_{hk} F_i(\mathbb{E}\left[\mathbf{X}\right]_t) \cdot COV\left[X_h X_k\right]_t$$

First-order equation for the average

$$\frac{d\mathbb{E}\left[X_i\right]_t}{dt} = F_i(\mathbb{E}\left[\mathbf{X}\right]_t)$$

SECOND-ORDER APPROXIMATION

EXACT EQUATION FOR COVARIANCE

$$\frac{dCOV\left[X_iX_k\right]_t}{dt} = \mathbb{E}\left[D_{ik}(\mathbf{X})\right]_t + \mathbb{E}\left[(X_i - \mathbb{E}\left[X_i\right]_t)F_k(\mathbf{X})\right]_t + \mathbb{E}\left[(X_k - \mathbb{E}\left[X_k\right]_t)F_i(\mathbf{X})\right]_t$$

SECOND-ORDER EQUATIONS FOR AVERAGE AND COVARIANCE

$$\frac{d\mathbb{E}\left[X_i\right]_t}{dt} = F_i(\mathbb{E}\left[\mathbf{X}\right]_t) + \frac{1}{2}\sum_{h,k=1}^{|T(N)|} \partial^2_{hk} F_i(\mathbb{E}\left[\mathbf{X}\right]_t) \cdot COV\left[X_hX_k\right]_t$$

$$\begin{aligned}\frac{dCOV\left[X_iX_k\right]_t}{dt} \quad = \quad & D_{ik}(\mathbb{E}\left[\mathbf{X}\right]_t) + \sum_{h=1}^{|\mathbf{X}|} \partial_h F_k(\mathbb{E}\left[\mathbf{Y}\right]_t) \cdot COV\left[X_iX_h\right]_t \\ & + \sum_{h=1}^{|\mathbf{X}|} \partial_h F_i(\mathbb{E}\left[\mathbf{X}\right]_t) \cdot COV\left[X_kX_h\right]_t\end{aligned}$$

Random walk

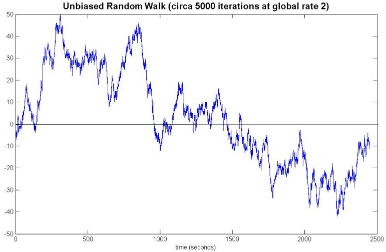
One variable $X \in \mathbb{Z}$.
Transitions: $(inc, \top, X' = X + 1, k)$, $(dec, \top, X' = X - 1, k)$

$F(X) = 0$
$D(X) = 2k$

$$\begin{cases} \dot{\mathbb{E}[X]} = F(\mathbb{E}[X]) + \frac{1}{2} COV\left[X^2\right] \partial^2_{XX} F(\mathbb{E}[X]) = 0 \\ \dot{COV}[X^2] = D(\mathbb{E}[X]) + 2COV\left[X^2\right] \partial_X F(\mathbb{E}[X]) = 2k \end{cases}$$

$$\mathbb{E}[X]_t = X_0$$

$$COV\left[X^2\right]_t = 2kt + COV\left[X_0^2\right]$$



Outline

The Linear Noise Ansatz

Fluctuations around the counting process are of order $N^{\frac{1}{2}}$. We assume that the PCTMC at level N fluctuates around the solution of the fluid equation:

$$\mathbf{X}^{(N)}(t) \approx N\mathbf{x}(t) + N^{\frac{1}{2}}\xi,$$

where ξ is a continuous random variable. This means that

$$\hat{\mathbf{X}}^{(N)}(t) \approx \mathbf{x}(t) + N^{-\frac{1}{2}}\xi$$

DERIVING THE EQUATIONS

One proceeds as follows

1. Write the master equation in terms of normalized variables;
2. Apply the Ansatz
3. Expand probability and propensity functions around $\mathbf{x}(t)$. This makes sense if $N^{-\frac{1}{2}}\xi$ is small.
4. Introduce a new probability density $\Pi(\mathbf{x}, t)$ for the noise term ξ
5. Collect terms in order $\frac{1}{2}$ of N to get the fluid equation for $\mathbf{x}(t)$, and in order 0 of N to get the PDE equation for Π.

Linear Noise Approximation

Drift, Jacobian, Diffusion matrix

$$F(\mathbf{x}) = \sum_{\eta \in \mathcal{T}} \mathbf{v}_\eta f_\eta(\mathbf{x})$$

$$J_{ij}(t) = \sum_{\eta \in \mathcal{T}} \mathbf{v}_\eta[i] \partial_j f_\eta(\mathbf{x}(t))$$

$$D_{ik}(\mathbf{x}) = \sum_{\eta \in \mathcal{T}} \mathbf{v}_\eta[i] \mathbf{v}_\eta[k] f_\eta(\mathbf{x})$$

Noise: Linear Fokker-Plank equation

$$\frac{\partial \Pi(\mathbf{x}, t)}{\partial(t)} = \sum_{i,j} J_{i,j}(t) \partial_i(\xi_j \Pi(\mathbf{x}, t)) + \frac{1}{2} \sum_{i,j} D_{ij} \partial_{ij} \Pi(\mathbf{x}, t).$$

LINEAR NOISE APPROXIMATION

LINEAR FOKKER-PLANK EQUATION

Linear Fokker-Plank equations have solutions which are Gaussian Processes! We can obtain the equations for average and variance from Π, and solve them to fully determine the noise term $\xi(t)$.

AVERAGE

$\frac{d\mathbb{E}[\xi(t)]}{dt} = J\mathbb{E}\left[\xi(t)\right]$, So if $\mathbb{E}\left[\xi(0)\right] = 0$, then $\mathbb{E}\left[\xi(t)\right] = 0$.

COVARIANCE MATRIX C

$$\frac{dC}{dt} = JC + CJ^T + D$$

SOLUTION TO THE SYSTEM

$\hat{\mathbf{X}}^{(N)}(t) \approx \mathbf{x}(t) + N^{-\frac{1}{2}}\xi(t)$ is a Gaussian Process.
At time t, it is a multivariate Gaussian distribution with mean $\mathbf{x}(t)$ and covariance $N^{-1}C$.

CENTRAL LIMIT THEOREM

We can look at the linear noise approximation from a limit theorem point of view.

$$\mathbf{X}^{(N)}(t) = N\mathbf{x}(t) + N^{\frac{1}{2}}\xi^{(N)}(t),$$

where we defined

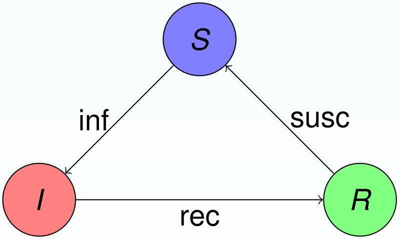
$$\xi^{(N)}(t) = N^{-\frac{1}{2}}(\mathbf{X}^{(N)}(t) - N\mathbf{x}(t))$$

CENTRAL LIMIT THEOREM (KURTZ)

If rate functions are of class C^1, then

$$\xi^{(N)} \Rightarrow \xi \text{ (weakly)}$$

EXAMPLE: SIR EPIDEMICS



Three variables: X_S,X_I,X_R.
State space:
$\mathcal{D} = \{(n_1, n_2, n_3) \mid n_1 + n_2 + n_3 = N\} \subset \{0, \ldots, N\}^3$.

Transitions:

- $(inf, \top, (-1, 1, 0) k_I \frac{X_I}{N} X_S)$
- $(rec, \top, (0, -1, 1), k_R X_I)$
- $(susc, \top, (1, 0, -1), k_S X_R)$

EXAMPLE: SIR EPIDEMICS

REDUCE THE SYSTEM DIMENSION

As $X_R = N - X_S - X_I$, we can reduce to two dimensions: $x_S = x$ and $x_I = y$. Call also $u = VAR(\xi_S)$, $v = VAR(\xi_I)$, $c = COV(\xi_S, \xi_I)$

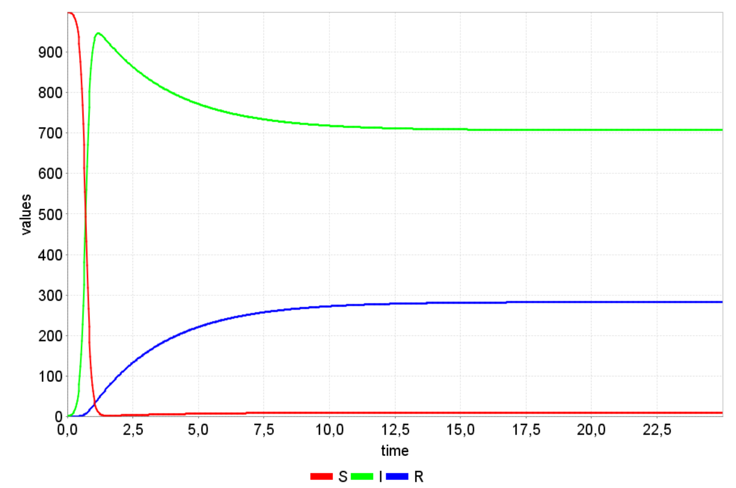
AVERAGE: FLUID EQUATIONS

$$\frac{dx}{dt} = -k_I xy + k_S(1 - x - y)$$
$$\frac{dy}{dt} = k_I xy - k_R y$$

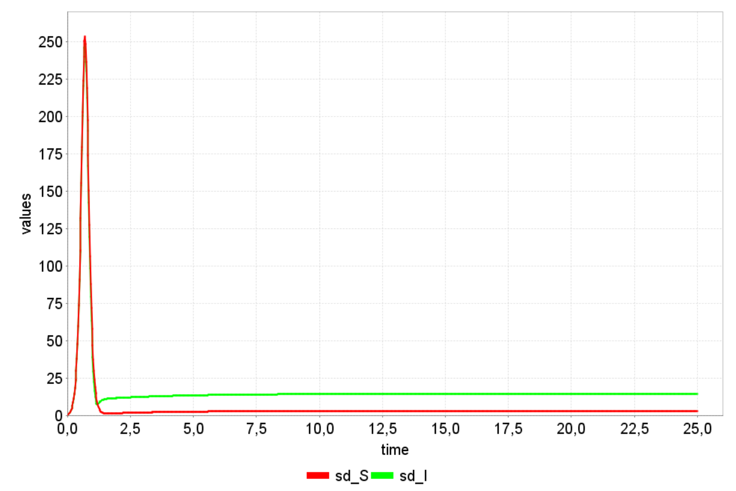
VARIANCE u OF x, v OF y, COVARIANCE c

$$\frac{du}{dt} = -2u(k_i y + k_s) - 2c(k_i x + k_s) + k_i xy + k_s(1 - x - y)$$
$$\frac{dv}{dt} = 2c(k_i y) + 2v(k_i x - kr) + kixy + k_r y$$
$$\frac{dc}{dt} = -c(k_i y + k_s) - v(k_i x + k_s) + k_i yu + c(k_i x - k_r) - k_i xy$$

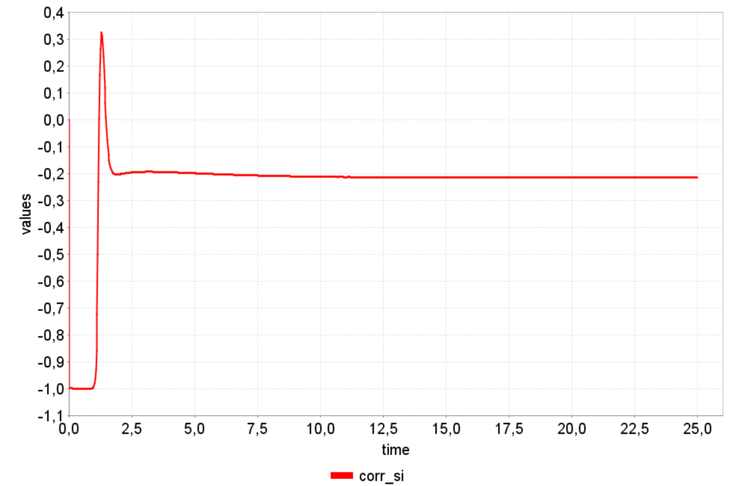
SIR EPIDEMICS: FLUID EQUATIONS



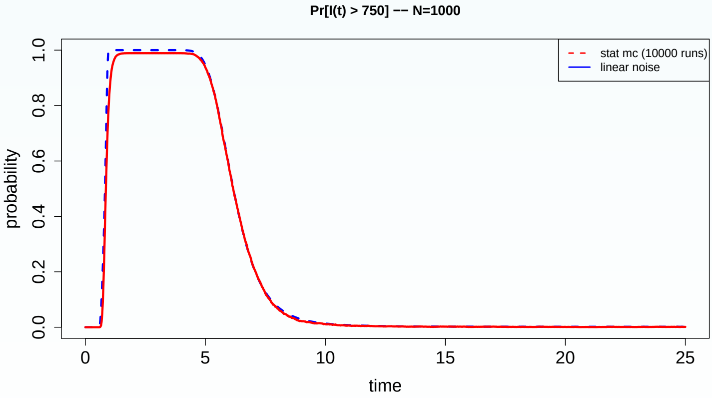
SIR EPIDEMICS: LN ESTIMATED STANDARD DEVIATION OF S AND I



SIR epidemics: LN estimated correlation of S and I



SIR EPIDEMICS: LN ESTIMATED $\mathbb{P}\{I(t) \geq 750\}$



REFERENCES

- T. Kurtz, S. Ethier, Markov Processes - Characterisation and Convergence, Wiley, 1986.
- L. Bortolussi, J. Hillston, D. Latella, M. Massink. Continuous Approximation of Collective Systems Behaviour: a Tutorial. Submitted to Performance Evaluation.
- A. Singh, J.P. Hespanha. *Lognormal moment closures for bio-chemical reactions*, Proc. of IEEE CDC 2006.
- J. Bradley, R. Hayden. *A Fluid analysis framework for a Markovian Process Algebra*, Theor. Comp. Science, 2010.
- Luca Bortolussi: On the Approximation of Stochastic Concurrent Constraint Programming by Master Equation. Electr. Notes Theor. Comput. Sci. 220(3): 163-180 (2008)
- Elf, J and Ehrenberg, M (2003) Fast evaluation of fluctuations in biochemical networks with the linear noise approximation Genome Research 13, 2475-2484.
- Grima R. 2010. An effective rate equation approach to reaction kinetics in small volumes: theory and application to biochemical reactions in nonequilibrium steady-state conditions. Journal of Chemical Physics, 133.