Limitations of the Van Kampen approach for stochastic epidemiological model

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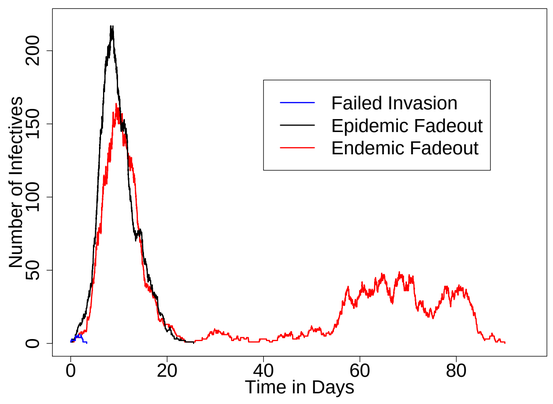
Stochastic Extinctions

In epidemiology, demographic stochasticity can lead to:

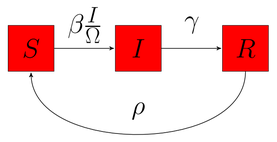


- Failed Invasion (due to the small number of individuals infected at the beginning of disease invasion, even if $R_0 > 1$ [1]).
- Epidemic Fadeout (extinction that occurs after a major outbreak depletes the available number of susceptibles).
- Endemic Fadeout (extinction from a relatively stable endemic state due to random fluctuations).

FIGURE 1: Evolution of the number of infectives for 3 different epidemic scenarios with same initiale conditions and stochastic demography ($SIRS$ model with $R_0 = 2$)

Markov Model

We use a simple markovian $SIRS$ model without death or natality.



- S, I, R : number of Susceptibles, Infectives and Recovered.
- $\Omega = S + I + R$ constant population size.

Under classical markovian hypothesis we can formulate the three transition rates:

- Infection: $T(S-1, I+1|S, I) = \beta\frac{\mathbf{I}}{\mathbf{\Omega}}$; non-linearity due to contact process.
- Recovery and Immunity: $T(S, I-1|S, I) = \gamma I$; mean infection period=$1/\gamma$.
- Loss of Immunity: $T(S+1, I|S, I) = \rho R = \rho(\Omega - S - I)$; mean immunity period=$1/\rho$.

The evolution of the probability distribution $P_{s,i}(t)$ over the state space $\{(S, I) \in \mathbb{N}^2, S + I \leq \Omega\}$ is governed by the following Master Equation:

$$\frac{\mathbf{dP_{s,i}(t)}}{\mathbf{dt}} = \beta\frac{\mathbf{(i-1)}}{\mathbf{\Omega}}\mathbf{(s+1)P_{s+1,i-1}(t)} + \gamma\mathbf{(i+1)P_{s,i+1}(t)} + \rho\mathbf{(\Omega-(s-1)-i)P_{s-1,i}(t)} - (\beta\frac{\mathbf{i}}{\mathbf{\Omega}}\mathbf{s} + \gamma\mathbf{i} + \rho\mathbf{(\Omega-s-i)})\mathbf{P_{s,i}(t)}$$

Analytical Approximation via Van Kampen Expansion

If $\forall t\ S_t \sim \Omega$ and $I_t \sim \Omega$ then we can expect system fluctuations to be of the order of $\sqrt{\Omega}$:

$$\begin{cases} S = \Omega\phi(t) + \sqrt{\Omega}\eta_1 \\ I = \Omega\theta(t) + \sqrt{\Omega}\eta_2 \end{cases}$$

- $\phi(\mathbf{t})$ and $\theta(\mathbf{t})$ are deterministic variables.
- $\eta_\mathbf{1}$ and $\eta_\mathbf{2}$ are random variables.

We can express the Master Equation in terms of the new random variables: η_1, η_2. Expanding the right-hand side of the resultant expression into a Taylor's series in $1/\sqrt{\Omega}$ we obtain, at the next to leading order [3]:

A system of ordinary differential equations governing the deterministic variables $\phi(t)$ and $\theta(t)$.

$$\begin{cases} \frac{\partial\phi}{\partial t} = -\beta\phi(t)\theta(t) + \rho(1 - \phi(t) - \theta(t)) \\ \frac{\partial\theta}{\partial t} = \beta\phi(t)\theta(t) - \gamma\theta(t) \end{cases}$$

NB: This is the classical deterministic $SIRS$ model.

A linear Fokker-Planck equation signifying that the fluctuations η_1 and η_2 of the system are gaussian centered. Fluctuation second order moments are governed by a system of ordinary differential equations.

$$\begin{cases} \frac{\partial E[\eta_1^2]}{\partial t} = -2(\beta\theta(t) + \rho)E[\eta_1^2] - 2(\beta\phi(t) + \rho)E[\eta_1\eta_2] \\ \qquad + \beta\phi(t)\theta(t) + \rho(1 - \phi(t) - \theta(t)) \\ \frac{\partial E[\eta_2^2]}{\partial t} = 2(\beta\phi(t) - \gamma)E[\eta_2^2] + 2\beta\theta(t)E[\eta_1\eta_2] + \beta\phi(t)\theta(t) + \gamma\theta(t) \\ \frac{\partial E[\eta_1\eta_2]}{\partial t} = \beta\theta(t)E[\eta_1^2] - (\beta\phi(t) + \rho)E[\eta_2^2] \\ \qquad + [\beta(\phi(t) - \theta(t)) - \gamma - \rho]E[\eta_1\eta_2] - \beta\phi(t)\theta(t) \end{cases}$$

Exact Approach via Numerical Integration

The Master Equation is linear in $P_{s,i}(t)$, we can therefore rewrite it:

$$\begin{cases} \frac{dP}{dt} = AP \\ P(t=0) = P_0 \end{cases} \text{ which solution is simply } P(t) = e^{tA}P_0$$

A is the transition matrix (size $\sim \frac{1}{4}\Omega^4$) between all the possible states and P is the vector (size $\sim \frac{1}{2}\Omega^2$) of the probabilities over all the state space.

As A is a large sparce matrix, we used the routine package EXPOKIT [2] that considers the serie's expansion of the solution:

$$P(t) = e^{tA}P_0 = P_0 + \frac{(tA)}{1!}P_0 + \frac{(tA)^2}{2!}P_0 + ...$$

The basic idea of the method is to approximate the solution by an element of the Krylov basis:

$$\mathscr{K}_m(tA, P_0) = Vect\{P_0, (tA)P_0, ..., (tA)^{m-1}P_0\} \text{ where usually } m \leq 50$$

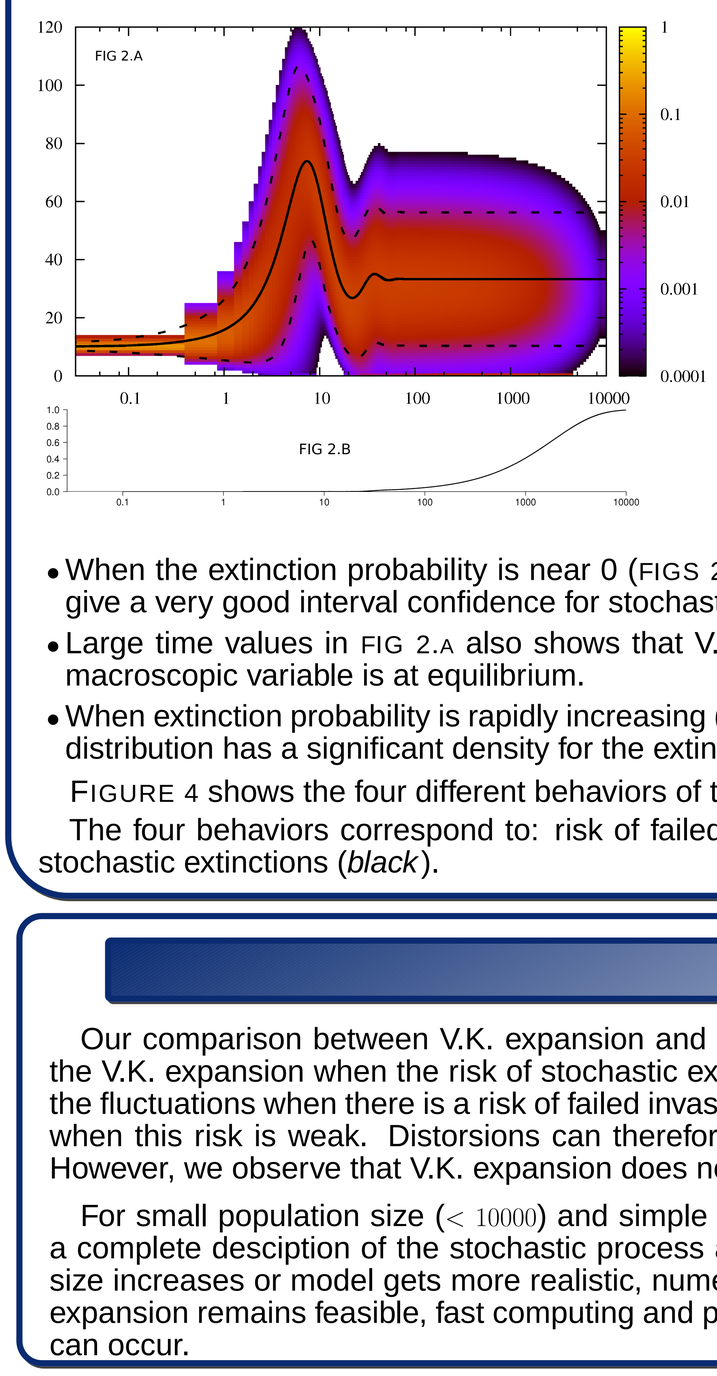
With this algorithm we just need to stock a workspace vector, size $\sim \frac{m}{2}\Omega^2$, instead of the whole transition matrix A whose size becomes too large since $\Omega > 100$.

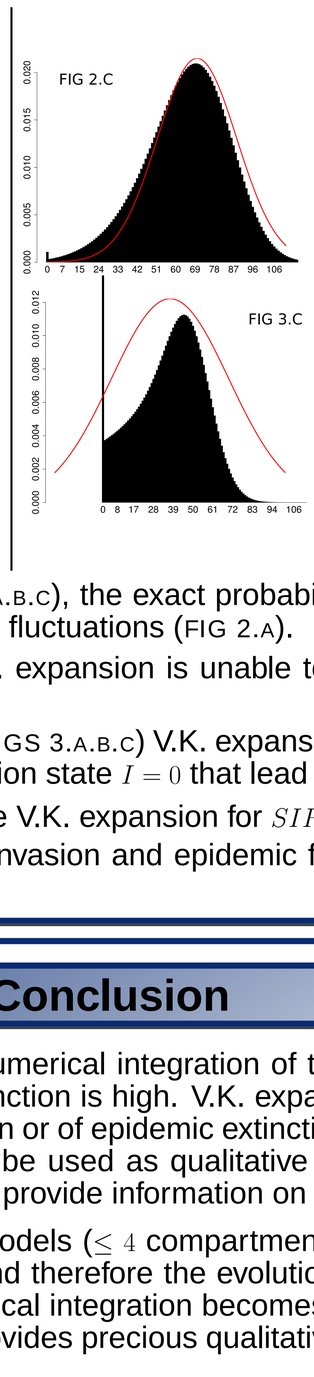
Comparison of the two Methods

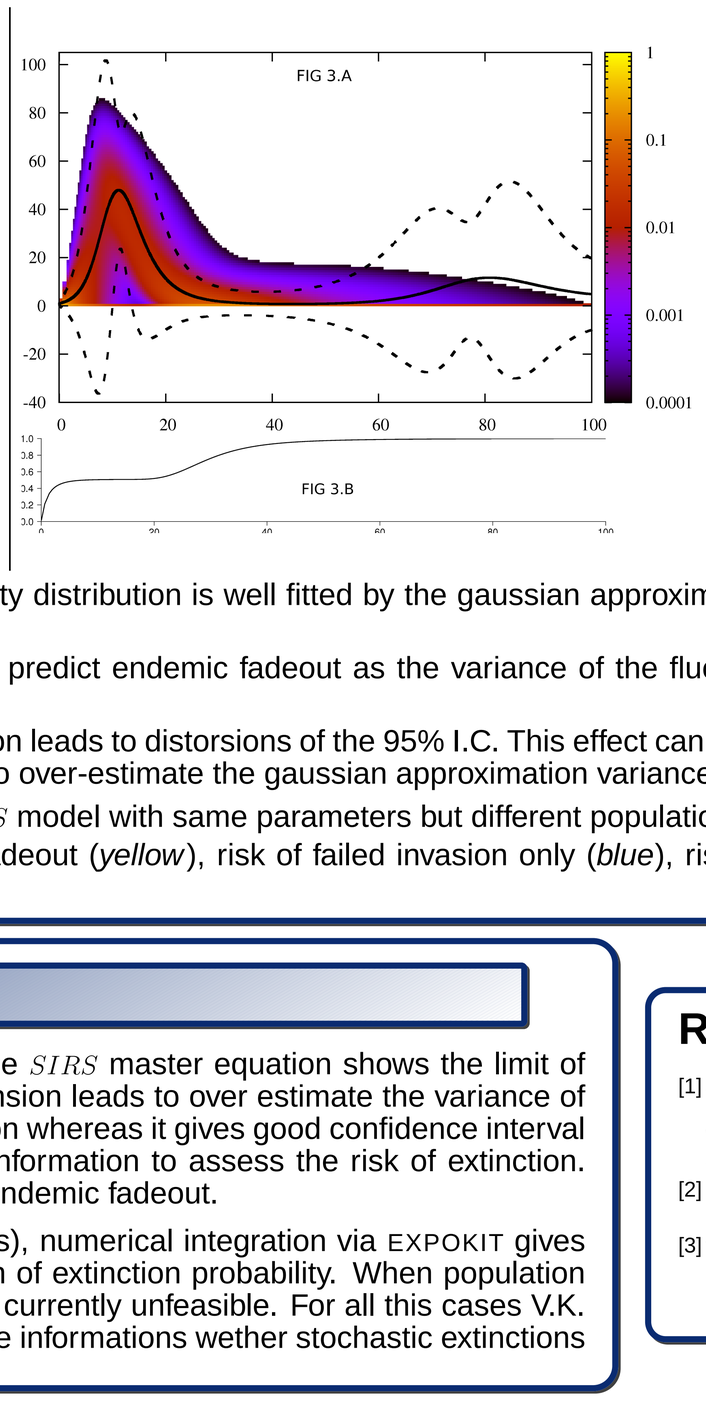
FIGURES 2.A AND 3.A: Evolution of the probability distribution of I_t (colored map) computed via EXPOKIT and the macroscopic variable (solid line) with 95% confidence interval (dashed lines) computed via Van Kampen (V.K.) expansion. In FIG 2.A time axis (days) is in logscale. FIG 2.A: $\Omega = 400, I_0 = 10, \rho = 0.1$ and FIG 3.A: $\Omega = 300, I_0 = 1, \rho = 0.02$

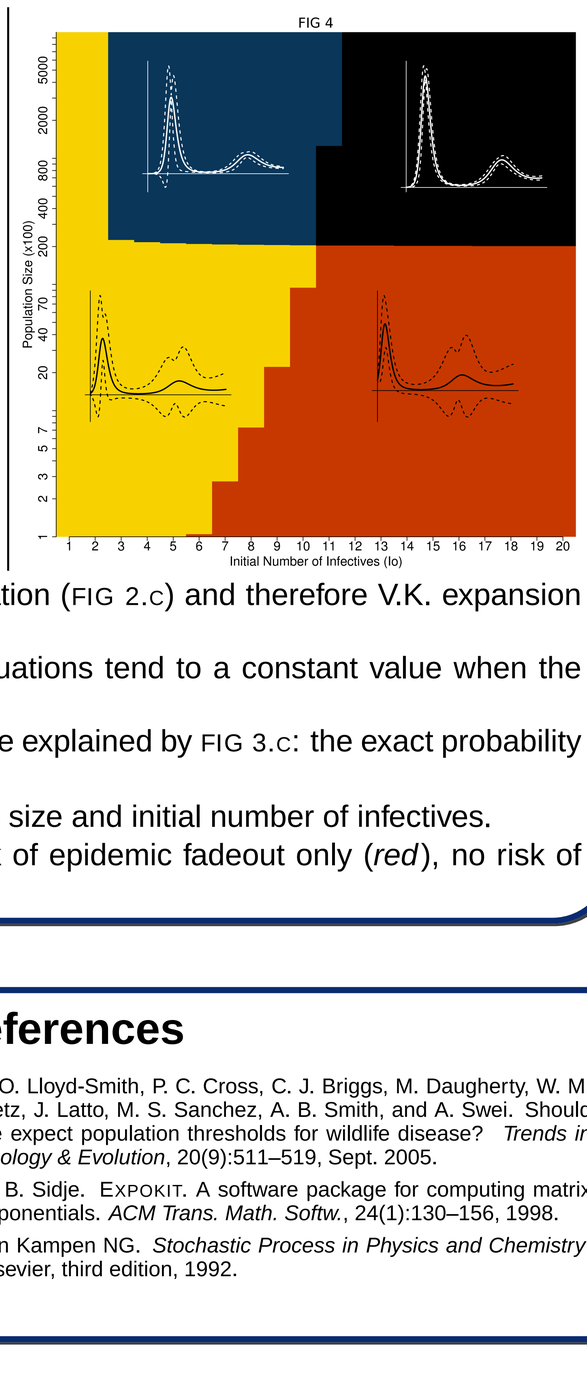
FIGURES 2.B AND 3.B: Evolution of the extinction probability $P(I = 0, t)$ computed via EXPOKIT. In FIG 2.B time axis (days) is in logscale.

FIGURES 2.C AND 3.C: (transversal cut of FIG 2.A and FIG 3.A) Comparison of the exact probability distribution with the gaussian approximation.









- When the extinction probability is near 0 (FIGS 2.A.B.C), the exact probability distribution is well fitted by the gaussian approximation (FIG 2.C) and therefore V.K. expansion give a very good interval confidence for stochastic fluctuations (FIG 2.A).
- Large time values in FIG 2.A also shows that V.K. expansion is unable to predict endemic fadeout as the variance of the fluctuations tend to a constant value when the macroscopic variable is at equilibrium.
- When extinction probability is rapidly increasing (FIGS 3.A.B.C) V.K. expansion leads to distorsions of the 95% I.C. This effect can be explained by FIG 3.C: the exact probability distribution has a significant density for the extinction state $I = 0$ that lead to over-estimate the gaussian approximation variance.

FIGURE 4 shows the four different behaviors of the V.K. expansion for $SIRS$ model with same parameters but different population size and initial number of infectives.

The four behaviors correspond to: risk of failed invasion and epidemic fadeout (*yellow*), risk of failed invasion only (*blue*), risk of epidemic fadeout only (*red*), no risk of stochastic extinctions (*black*).

Conclusion

Our comparison between V.K. expansion and numerical integration of the $SIRS$ master equation shows the limit of the V.K. expansion when the risk of stochastic extinction is high. V.K. expansion leads to over estimate the variance of the fluctuations when there is a risk of failed invasion or of epidemic extinction whereas it gives good confidence interval when this risk is weak. Distorsions can therefore be used as qualitative information to assess the risk of extinction. However, we observe that V.K. expansion does not provide information on endemic fadeout.

For small population size (< 10000) and simple models (≤ 4 compartments), numerical integration via EXPOKIT gives a complete desciption of the stochastic process and therefore the evolution of extinction probability. When population size increases or model gets more realistic, numerical integration becomes currently unfeasible. For all this cases V.K. expansion remains feasible, fast computing and provides precious qualitative informations wether stochastic extinctions can occur.

References

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