# A Markov model for the spread of hepatitis C virus

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## Objectives

- A model of the spread of HCV with Markov processes.
- Finding a deterministic differential system of the model.
- Asymptotic analysis.
- A mean-field approximation of the process.
- Limit of the prevalence.
- Even for a small value of N, finding a concordance between the prevalence observed with the stochastic model and the deterministic limit.

## The model

- $X_1(t)$ and $X_2(t)$ the number of antibody - positive (AP), respectively of antibody - negative (AN), drug users of a population.
- Aps and ANs arrive continuously according to a Poisson process of intensity $r$, respectively $\lambda$. A given drug user has the probability of being AP : of $q(t) = X_1(t)(X_1(t) + X_2(t))$.
- Aps and ANs exits by death or self - healing under an exponentially distributed time of parameter $\mu_1$, respectively $\mu_2$

For medical reasons, the probability of being infected even in such case is denoted by $p_I$. Thus, the global probability of being infected is $pq(t)$ with $p$ another parameter to be estimated. We call $\alpha$ the rate at which a drug user injects.

So the transitions are :

- $q_1(n_1, n_2) = r + \lambda p_I \frac{n_1}{n_1+n_2}$
- $q_2(n_1, n_2) = \mu_1 n_1$
- $q_3(n_1, n_2) = \alpha p n_2 \frac{n_1}{n_1+n_2}$
- $q_4(n_1, n_2) = \lambda(1 - p_I \frac{n_1}{n_1+n_2})$
- $q_5(n_1, n_2) = \mu_2 n_2$.

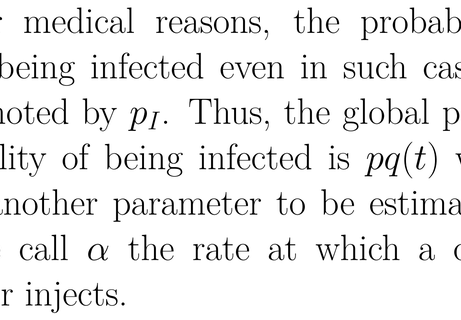


Figure 1: Transitions of the Markov model

## A deterministic differential system

According to the model, the situation can be described by this system :

$$(S_r(x^0)) \quad \begin{cases} \psi_1'(t) &= r + \lambda p_I \frac{\psi_1(t)}{\psi_1(t)+\psi_2(t)} \\ &\quad -\mu_1\psi_1(t) + \alpha p \frac{\psi_1(t)\psi_2(t)}{\psi_1(t)+\psi_2(t)}, \\ \psi_1(0) &= x_1^0, \\ \psi_2'(t) &= \lambda(1 - p_I \frac{\psi_1(t)}{\psi_1(t)+\psi_2(t)}) \\ &\quad -\mu_2\psi_2(t) - \alpha p \frac{\psi_1(t)\psi_2(t)}{\psi_1(t)+\psi_2(t)}), \\ \psi_2(0) &= x_2^0. \end{cases}$$

For any non zero initial conditions, there exists a unique solution with the following invariant points :

(a) $\xi_1 = \frac{ab-c+sgn(a)\sqrt{(ab-c)^2+4abr\mu_1}}{2a\mu_1}$,
(b) $\xi_2 = \frac{1}{\mu_2}(r + \lambda - \mu_1\xi_1)$,
With $a = \alpha p - \mu_1 + \mu_2$,
$b = r + \lambda$ ,
and $c = r\mu_1 + \lambda(1 - p_I)\mu_2$.

## Important Result

Thanks to the convergence described by Equation 4, we find that our markov model can be described accurately by the solution of the differential system $(S_r(x^0))$.

## Mean Field Approximation

If we consider the sequence $(X^N(t) = (X_1^N(t), X_2^N(t))_{t\hat{a}L\check{e}0}$ of Markov processes and if we replace the rates with respectively $\lambda_n$ and $r_N$, we obtain the following theorem :
Under these assumptions:

$$\mathbb{E}\left[\left\|\frac{1}{N}X^N(0) - x^0\right\|^2\right] \overset{N\to}{\to}^{+\infty} 0 \qquad (1)$$

$$\frac{1}{N}r_N \overset{N\to}{\to}^{+\infty} r \geq 0 \qquad (2)$$

$$\frac{1}{N}\lambda_N \overset{N\to}{\to}^{+\infty} \lambda \qquad (3)$$

We have, with $\psi(x^0, .) = (\psi_1(x^0, .), \psi_2(x^0, .))$ the solution of the differential system $(S_r(x^0))$, for any T > 0 :

$$\mathbb{E}\left[sup_{t\leq T}\left\|\frac{1}{N}X^N(t) - \psi(x^0, t)\right\|^2\right] \overset{N\to}{\to}^{+\infty} 0 \qquad (4)$$

(4) means that for a large population the process X is close to the solution $\psi$ of the deterministic differential system.

## Stationary regime

- $X^N = (X_1^N, X_2^N)$ has a limiting distribution when N tends to infinity.
- $\frac{X^N}{N} \overset{N\to}{\to}^{\infty} \psi^\infty(t)$.
- $\psi^\infty(t) \overset{t\to}{\to}^{\infty} \psi^\infty$ a real.

Thus, the limiting distribution converges to the Dirac mass at $\psi^\infty$ when N tends to infinity. In other words, the following diagram is established, with $Y^N = \frac{X^N}{N}$ :

$$\begin{array}{ccc} \mathbf{P}_{Y^N(t),\delta_{x^0}} & \xrightarrow{N\to\infty} & \mathbf{P}_{\psi(t),\delta_{x^0}} \\ \downarrow{\scriptstyle t\to\infty} & & \downarrow{\scriptstyle t\to\infty} \\ \mathbf{P}_{Y^N(\infty)} & \xrightarrow[N\to\infty]{} & \delta_{\psi^\infty} \end{array}$$

Figure 2: Limits and stationary regime

## Results of the numerical computation

Here is a simulation of the Markov process for N = 100 and the estimate of the prevalence by a Monte - Carlo method on 1000 trajectories, with the parameters $\alpha = 1$, $\mu_1 = 0.1$, $\mu_2 = 0.2$, $r = 1$, $\lambda = 5$ and $p_I = 0.8$.


Figure 3: Prevalence with respect to p

The solid line represents the value as computed by the invariant points $\xi_1$ and $\xi_2$. The dots represents the simulated values according to the Markov model. So the convergence described by (4) is quick.

## Why those parameters ?

The choice of the parameters was delicate as biological parameters are not very well known and population dependent quantities are even more harsh to determine. Thus we choose parameters which seemed reasonable and we computed the following result of the differential system :

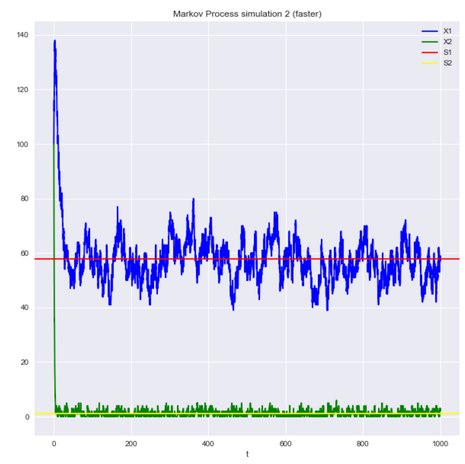


Figure 4: $X_1$ and $X_2$ as time goes by

One could expect such curve for this situation. With really different parameters the result was less credible : we observed too many or too few individuals in each population, or with numerous and unlikely upheavals, especially if $\mu_1$ ou $\mu_2$ are too high.

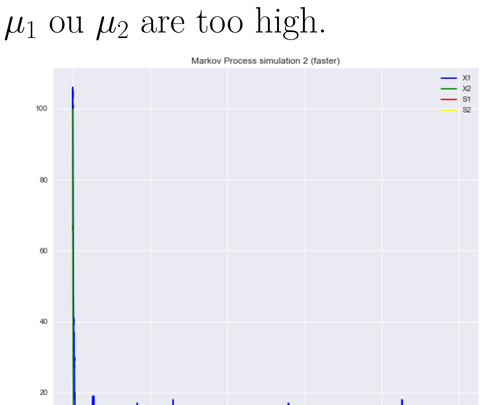


Figure 5: $X_1$ and $X_2$ with high $mu_1$ and $mu_2$

## References

This was made for the class MACS207a on stochastic calculus at Telecom Paristech. All the data and calculations are from "A Markov model for the spread of hepatitis C virus" by L.Coutin, L.Decreusefond and J.S. Dhersin.

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