Mathématiques et statistiques pour le modèle SIR en épidémiologie

Viet Chi TRAN - Université Lille 1 - France

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References


E. Pardoux et al. Lecture notes in prep.
Course 1: Stochastic compartmental SIR model

Course 2: SIR model on a random graph

Course 3: Statistical estimation for a compartmental SIR model
Compartmental SIR model (1)

★ Population of size $N + 1$.

★ Individuals are separated into 3 classes:
  ▶ Susceptibles $S_t$, size $S_t$ at time $t \geq 0$,
  ▶ Infectious $I_t$, size $I_t$,
  ▶ Removed $R_t$, size $R_t$.

★ Initial conditions $S_0 = N$, $I_0 = 1$.

★ $\forall t \geq 0$, $S_t + I_t + R_t = N + 1$. 

Compartmental SIR model (2)

★ Infection rate:
  ▶ Infectious individuals have infectious contacts at rate $\lambda$,
  ▶ The contact is chosen uniformly among the $N$ individuals

★ For a given pair with one infective and one susceptible, the rate at which the infective transmits the disease to the susceptible individual is $\lambda/N$.

★ Removal rate:
Each infective becomes removed at rate $\gamma$.

★ At the population level:
  ▶ The global infection rate at time $t$ is $\frac{\lambda}{N} S_t l_t$.
  ▶ The global recovery rate at time $t$ is $\gamma l_t$. 
Branching approximations
Start of the epidemic

★ Start from a single infective $I_0 = 1$ in a large population $N + 1$.

★ Infectious individuals have contacts at rate $\lambda$. The probability of contacting somebody who is susceptible is $\frac{S_t}{N}$.

★ As long as the infectives or removed are not contacted a second time, there is a coupling between $I_t$ and a continuous time branching process $(Z_t)_{t \geq 0}$ where
  ▶ individuals die at rate $\gamma$,
  ▶ they give birth at rate $\lambda$.

$Z_t$ is the population size at time $t$.

★ The first infective or removed that is contacted a second time is a ghost.
Branching approximation

★ The expectation of the offspring number \( Y \) is:

\[
\mathbb{E}(Y) = \mathbb{E}(\mathbb{E}(Y \mid \text{lifelength})) = \int_{0}^{\infty} (\lambda t) \gamma e^{-\gamma t} dt = \frac{\lambda}{\gamma} =: R_0.
\]

★ Define \( \tau = \text{inf}\{t \geq 0, \ Z_t = 0\} \).

★ The generating function of the offspring number \( Y \) is

\[
g(s) = \mathbb{E}(s^Y) = \sum_{k=0}^{\infty} s^k \mathbb{P}(Y = k) = \sum_{k=0}^{\infty} s^k \int_{0}^{\infty} \frac{\lambda^k t^k}{k!} e^{-\lambda t} \gamma e^{-\gamma t} dt \\
= \int_{0}^{\infty} \gamma \exp(-((1 - s)\lambda + \gamma) t) \\
= \frac{\gamma}{(1 - s)\lambda + \gamma}.
\]
Criticity of the branching process

\[ R_0 = \frac{\lambda}{\gamma} \]

★ Prop: The branching process \((Z_t)_{t \geq 0}\) is

- subcritical or critical if \(\lambda \leq \gamma\) \(\iff\) \(R_0 \leq 1\). Then \(\mathbb{P}(\tau < +\infty) = 1\).
- supercritical if \(\lambda > \gamma\) \(\iff\) \(R_0 > 1\).

Then \(\mathbb{P}(\tau < +\infty) = p \in (0, 1)\) where \(p\) is solution of \(p = g(p)\)

\[ \iff \lambda(p - 1)(p - \frac{\gamma}{\lambda}) = 0 \iff p = \frac{\gamma}{\lambda} \]

and \(\mathbb{P}(\lim_{t \to +\infty} Z_t = +\infty) = p.\)
The branching process and the epidemic process agree until time $T_N$, where the first ghost appears.

Define $M_N$ the number of infections before the first ghost, so that the ghost corresponds to the $M_N + 1$-th birth in the tree.

**Prop:** $\mathbb{P}(M_N > k) = 1 - \frac{k(k+1)}{2N} + k^2 O\left(\frac{1}{N}\right)$.

**Proof:**

\[
\mathbb{P}(M_N > k) = \prod_{j=1}^{k+1} \left( 1 - \frac{j-1}{N} \right) = 1 - \sum_{j=0}^{k} \frac{j}{N} + k^2 O\left(\frac{1}{N^2}\right).
\]

So as long as $k(N) = o(\sqrt{N})$, $\lim_{N \to +\infty} \mathbb{P}(M_N > k(N)) = 1$. 

Let \( A_t \) be the number of births in the branching process before \( t \).

It is known that \( A(t) = O(e^{rt}) \) where the Malthus parameter \( r \) is defined by:

\[
\int_0^{+\infty} e^{-rt} \lambda e^{-\gamma t} \, dt = 1 \iff r = \lambda - \gamma.
\]

Hence, for \( \varepsilon > 0 \), there exists \( C_\varepsilon > 0 \) such that

\[
1 - \varepsilon \leq \lim_{N \to +\infty} \mathbb{P}(k(N) \leq C_\varepsilon e^{rT_N})
\]

from which we deduce:

\[
\lim_{N \to +\infty} \mathbb{P}(T_N \geq \frac{\log(k(N)) - \log(C_\varepsilon)}{r}) \geq 1 - \varepsilon.
\]
Total size of the epidemic for $R_0 < 1$

★ $K$ is the size of epidemic when it dies out.

★ Let $(Y_n)_{n \in \mathbb{N}^*}$ be i.i.d. random variables with the distribution of $Y$ (generating function $g$).

★ **Prop:** for all $k \in \mathbb{N}^*$,

$$
\mathbb{P}(K = k) = \frac{1}{k} \mathbb{P}(Y_1 + \cdots + Y_k = k - 1).
$$

*Proof:* Consider the exploration process of the tree corresp. to $(Y_n)_{n \in \mathbb{N}^*}$:

- individuals are ranked in lexicographical order (see contour process),
- The offspring number of the $n$-th vertex is $Y_n$.
- Then: $H_0 = 1$, $H_n = 1 + \sum_{i=1}^{n} (Y_i - 1)$.

The tree is encoded by an excursion from 1 which returns at 0 when all nodes have been explored.

To each excursion of length $k$, where the increments are $\geq -1$, we can associate (by permutation of the $Y_i$'s) $k$ trajectories such that

$$1 + \sum_{i=1}^{k} (Y_i - 1) = 0 \iff \sum_{i=1}^{k} Y_i = k - 1.$$

To each sequence of $k$ integers $\geq -1$ such that $\sum_{i=1}^{k} Y_i = k - 1$, there exists a single permutation that corresponds to an excursion.
Total size of the epidemic for $R_0 < 1$

★ $K$ is the size of epidemic when it dies out.

★ Let $(Y_n)_{n \in \mathbb{N}^*}$ be i.i.d. random variables with the distribution of $Y$ (generating function $g$).

★ **Prop:** for all $k \in \mathbb{N}^*$,

$$\mathbb{P}(K = k) = \frac{1}{k} \mathbb{P}(Y_1 + \cdots + Y_k = k - 1).$$

★ **Examples:**

If $Y$ follows a Poisson distribution of parameter $\alpha$, $Z_\tau$ follows a Borel distribution:

$$\mathbb{P}(K = k) = \frac{(\alpha k)^{k-1}}{k!} e^{-\alpha k}.$$

If $Y + 1$ follows a Geometric distribution of parameter $\rho$, $k + \sum_{i=1}^{k} Y_i$ follows a negative binomial, from which:

$$\mathbb{P}(K = k) = \frac{(2k - 2)!}{k!(k - 1)!} \rho^k (1 - \rho)^{k-1}.$$
Stochastic Differential Equations
Random point events

★ **Def:** A Poisson point process $Q(ds, d\theta)$ on $\mathbb{R}_+^2$ with intensity measure $q(ds, d\theta)$ is a random point measure on $\mathbb{R}_+^2$ such that

- For all $A \in \mathcal{B}(\mathbb{R}_+^2)$, $Q(A)$ is distributed as a Poisson random variable with parameter $q(A)$.
- For all finite family of disjoint measurable subsets $(A_i)_{i \in I}$, $(Q(A_i))_{i \in I}$ is a family of independent random variables.
Counting processes

★ Let $Q(ds, d\theta)$ be a Poisson point measure with intensity $ds \, d\theta$.

Assume that $t \in \mathbb{R}_+ \mapsto \lambda(t) \in \mathbb{R}_+$ is a measurable map.

Then

$$M_t = \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \lambda(s)} Q(ds, d\theta)$$

is a càdlàg counting process with the following properties on the times of jump:

$$\mathbb{P}(T_{k+1} - T_k > t | T_k) = \exp \left( - \int_0^t \lambda(T_k + s)ds \right)$$

Hence, conditionally to $T_k$, the distribution of $T_{k+1}$ is

$$\lambda(T_k + t) \exp \left( - \int_0^t \lambda(T_k + s)ds \right).$$
Integrating against Poisson processes

Let \((\omega, t, \theta) \mapsto H(\omega; t, \theta)\) be a predictable process. Then:

\[
M_t = \int_0^t \int_{\mathbb{R}_+} H(t, \theta) Q(ds, d\theta) - \int_0^t \int_{\mathbb{R}_+} H(t, \theta) q(ds, d\theta)
\]

1) is a local martingale,
Integrating against Poisson processes

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\]

1) is a local martingale,

2) if \(\mathbb{E}\left( \int_0^t \int_{\mathbb{R}_+} |H(t, \theta)| q(ds, d\theta) \right) < +\infty\), then \((M_t)\) is a real martingale.

\[
\forall 0 < s < t, \quad \mathbb{E}(M_t | F_s) = M_s, \quad \mathbb{E}(M_t) = \mathbb{E}(M_0) = 0 \quad \text{and}
\]

\[
\mathbb{E}\left( \int_0^t \int_{\mathbb{R}_+} H(t, \theta) Q(ds, d\theta) \right) = \mathbb{E}\left( \int_0^t \int_{\mathbb{R}_+} H(t, \theta) q(ds, d\theta) \right).
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Integrating against Poisson processes

Let \( (\omega, t, \theta) \mapsto H(\omega; t, \theta) \) be a predictable process. Then:

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1) is a local martingale,

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\[
\forall 0 < s < t, \quad \mathbb{E}(M_t | \mathcal{F}_s) = M_s, \quad \mathbb{E}(M_t) = \mathbb{E}(M_0) = 0 \quad \text{and}
\]

\[
\mathbb{E}(\int_0^t \int_{\mathbb{R}_+} H(t, \theta)Q(ds, d\theta)) = \mathbb{E}(\int_0^t \int_{\mathbb{R}_+} H(t, \theta)q(ds, d\theta)).
\]

3) if \( \mathbb{E}(\int_0^t \int_{\mathbb{R}_+} |H(t, \theta)|^2 q(ds, d\theta)) < +\infty \), then \((M_t)\) is a square integrable martingale with previsible quadratic variation

\[
\langle M \rangle_t = \int_0^t \int_{\mathbb{R}_+} H^2(t, \theta) q(ds, d\theta).
\]

\[
\text{Var}(M_t) = \mathbb{E}(M_t^2) = \mathbb{E}(\langle M \rangle_t) = \mathbb{E}(\langle M \rangle_t) = \mathbb{E}(\int_0^t \int_{\mathbb{R}_+} H^2(t, \theta) q(ds, d\theta)).
\]
Let us consider two Poisson point measures $Q^1(ds, d\theta)$ et $Q^2(ds, d\theta)$ with intensity $ds \, d\theta$ sur $\mathbb{R}_+^2$.

\[
\begin{align*}
S_t &= S_0 - \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \frac{\lambda}{N} S_s - I_s} Q^1(ds, d\theta) \\
I_t &= I_0 + \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \frac{\lambda}{N} S_s - I_s} Q^1(ds, d\theta) - \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \gamma I_s} Q^2(ds, d\theta) \\
R_t &= R_0 + \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \gamma I_s} Q^2(ds, d\theta).
\end{align*}
\]
Stochastic differential equation

Let us consider two Poisson point measures $Q^1(ds, d\theta)$ et $Q^2(ds, d\theta)$ with intensity $ds \, d\theta$ sur $\mathbb{R}_+^2$.

\[
\begin{align*}
S_t &= S_0 - \int_0^t \frac{\lambda}{N} S_s I_s \, ds - M^1_t \\
l_t &= l_0 + \int_0^t \frac{\lambda}{N} S_s I_s \, ds - \int_0^t \gamma I_s \, ds + M^1_t - M^2_t \\
R_t &= R_0 + \int_0^t \gamma I_s \, ds + M^2_t
\end{align*}
\]

where

\[
M^1_t = \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \frac{\lambda}{N} S_s I_s} \, Q^1(ds, d\theta) - \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \frac{\lambda}{N} S_s I_s} \, ds \, d\theta,
\]

\[
M^2_t = \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \gamma I_s} \, Q^2(ds, d\theta) - \int_0^t \int_{\mathbb{R}_+} 1_{\theta \leq \gamma I_s} \, ds \, d\theta,
\]
Stochastic differential equation

Let us consider two Poisson point measures $Q^1(ds, d\theta)$ et $Q^2(ds, d\theta)$ with intensity $ds \, d\theta$ sur $\mathbb{R}^2_+$. 

\[
\begin{align*}
S_t &= S_0 - \int_0^t \frac{\lambda}{N} S_s I_s ds - M^1_t \\
I_t &= I_0 + \int_0^t \frac{\lambda}{N} S_s I_s ds - \int_0^t \gamma I_s ds + M^1_t - M^2_t \\
R_t &= R_0 + \int_0^t \gamma I_s ds + M^2_t
\end{align*}
\]

where

\[
M^1_t = \int_0^t \int_{\mathbb{R}^+} \mathbf{1}_{\theta \leq \frac{\lambda}{N} S_s - I_s} Q^1(ds, d\theta) - \int_0^t \frac{\lambda}{N} S_s I_s ds,
\]

\[
M^2_t = \int_0^t \int_{\mathbb{R}^+} \mathbf{1}_{\theta \leq \gamma I_s} Q^2(ds, d\theta) - \int_0^t \gamma I_s ds,
\]
Stochastic differential equation

Let us consider two Poisson point measures $Q^1(ds, d\theta)$ et $Q^2(ds, d\theta)$ with intensity $ds \, d\theta$ sur $\mathbb{R}^2_+$.

\[
\begin{align*}
S_t &= S_0 - \int_0^t \frac{\lambda}{N} S_s l_s ds - M^1_t \\
l_t &= l_0 + \int_0^t \frac{\lambda}{N} S_s l_s ds - \int_0^t \gamma l_s ds + M^1_t - M^2_t \\
R_t &= R_0 + \int_0^t \gamma l_s ds + M^2_t
\end{align*}
\]

where

\[
\langle M^1 \rangle_t = \int_0^t \frac{\lambda}{N} S_s l_s ds,
\]

\[
\langle M^2 \rangle_t = \int_0^t \gamma l_s ds,
\]

\[
\langle M^1, M^2 \rangle_t = 0.
\]
Large population limit

★ We consider the renormalized processes:

\[
S^N_t = \frac{S_t}{N}, \quad I^N_t = \frac{I_t}{N}, \quad R^N_t = \frac{R_t}{N}.
\]

\[
S^N_t + I^N_t + R^N_t = 1 + \frac{1}{N}.
\]

★ For the susceptible individuals:

\[
S_t = S_0 - \int_0^t \int_{\mathbb{R}^+} 1_{\theta \leq \frac{\lambda}{N} S_s I_s} Q^1(ds, d\theta)
\]

\[
S^N_t = S_0^N - \int_0^t \int_{\mathbb{R}^+} \frac{1}{N} 1_{\theta \leq \lambda N S^N_u I^N_u} Q^1(du, d\theta)
\]

\[
= S_0^N - \int_0^t \int_{\mathbb{R}^+} \lambda S^N_u I^N_u du - M^{1,N}_t.
\]

where \(M^{1,N}\) is a square integrable martingale with

\[
\langle M^{1,N} \rangle_t = \frac{1}{N^2} \int_0^t \lambda N S^N_u I^N_u du = \frac{1}{N} \int_0^t \lambda S^N_u I^N_u du
\]
Kermack McKendrick ODE

★ Assumptions:

$$\lim_{N \to +\infty} \left( S_N^t, I_N^t, R_N^t \right) = (s_0, i_0, r_0)$$

with \((s_0, i_0) \in (0, 1), \ r_0 \in [0, 1)\) and \(s_0 + i_0 + r_0 = 1\).

★ Prop: When \(N \to +\infty\), \((S^N, I^N, R^N)\) converges to the solution of

\[
\begin{align*}
    s_t &= s_0 - \int_0^t \lambda s_u i_u \, du \\
    i_t &= i_0 + \int_0^t \left( \lambda s_u i_u - \gamma i_u \right) du \\
    r_t &= r_0 \int_0^t \gamma i_u \, du.
\end{align*}
\]
Proof:
★ The process \((S^N, I^N, R^N)\) takes its values in \([0, 1 + \frac{1}{N}]^3 \subset [0, \frac{3}{2}]^3\).

★ Aldous criterion is satisfied for each component. Let \(T > 0, \varepsilon > 0\) and \(\eta > 0\). Let \((\tau_N, \sigma_N)\) be two stopping times such that \(\sigma_N \leq \tau_N \leq \min(T, \tau_N + \delta)\).

\[
\mathbb{E}(|S_{\tau_N}^N - S_{\sigma_N}^N|) = \mathbb{E}\left( |\int_{\sigma_N}^{\tau_N \wedge T} \lambda S_u^N I_u^N \, du + M_{\tau_N \wedge T}^{1,N} - M_{\sigma_N}^{1,N}| \right)
\leq \lambda \frac{9}{4} \delta + \mathbb{E}\left( |M_{\tau_N \wedge T}^{1,N} - M_{\sigma_N}^{1,N}| \right)
\leq \lambda \frac{9}{4} \delta + \sqrt{\mathbb{E}\left( |M_{\tau_N \wedge T}^{1,N} - M_{\sigma_N}^{1,N}|^2 \right)}
\leq \lambda \frac{9}{4} \delta + \sqrt{\mathbb{E}\left( \int_{\sigma_N}^{\tau_N \wedge T} \frac{\lambda}{N} S_u^N I_u^N \, du \right)}
\leq \lambda \frac{9}{4} \delta + \sqrt{\frac{\lambda}{N} \frac{9}{4} \delta} < \frac{\varepsilon}{\eta}
\]

for \(\delta\) sufficiently small and \(N\) sufficiently large.

By Markov inequality and because the upper bound does not depend on \(N\):
\[
\exists \delta_0 > 0, \exists N_0 \in \mathbb{N}^*,
\sup_{N \geq N_0} \mathbb{P}(|S_{\tau_N}^N - S_{\sigma_N}^N| > \eta) \leq \frac{1}{\eta} \mathbb{E}(|S_{\tau_N}^N - S_{\sigma_N}^N|) < \varepsilon.
\]
The limiting values satisfy the Kermack-McKendrick system:

\[
\begin{align*}
    s_t &= s_0 - \int_0^t \lambda s_u i_u \, du \\
    i_t &= i_0 + \int_0^t (\lambda s_u i_u - \gamma i_u) \, du \\
    r_t &= r_0 \int_0^t \gamma i_u \, du.
\end{align*}
\]

There is thus existence of the solution.

The solution is of class \( \mathcal{C}^\infty \) in \( t \), and the system can be rewritten in ODE form:

\[
\begin{align*}
    \frac{ds_t}{dt} &= -\lambda s_t i_t \\
    \frac{di_t}{dt} &= \lambda s_t i_t - \gamma i_t \\
    \frac{dr_t}{dt} &= \gamma i_t.
\end{align*}
\]

Uniqueness of the solution is ensured by Cauchy-Lipschitz theorem.
Kermack McKendrick ODE (2)

\[
\begin{align*}
\frac{ds_t}{dt} &= -\lambda s_t i_t \\
\frac{d\bar{s}_t}{dt} &= \lambda s_t i_t - \gamma \bar{s}_t \\
\frac{dr_t}{dt} &= \gamma \bar{s}_t,
\end{align*}
\]

with initial conditions \((s_0, i_0, r_0) \in (0, 1)^2 \times [0, 1)\) with \(s_0 + i_0 + r_0 = 1\).

- \(s_t\) is a decreasing function in time, \(r_t\) is an increasing function.
- \(s_t, i_t \) and \(r_t\) take their values in \([0, 1]\).
- The solution converges to a stationary value \((s_\infty, i_\infty, r_\infty)\) where \(i_\infty = 0\).
★ Prop:
\[
\log \left( \frac{S_t}{S_0} \right) = -\frac{\lambda}{\gamma} (r_t - r_0).
\]

Proof:
\[
\frac{s'(t)}{s(t)} = -\lambda i_t = -\frac{\lambda}{\gamma} r'(t).
\]

★ Prop: Assume that \( s_0 = 1 - \nu - \epsilon \), \( i_0 = \epsilon \) (small) and \( r_0 = \nu \). Define the fraction of susceptible that are infected by the end of the epidemic as
\[
Z_\epsilon = \frac{s_0 - s_\infty}{s_0} = \frac{r_\infty - r_0}{s_0} = \frac{r_\infty - r_0}{1 - \nu - \epsilon}.
\]

Then:
\[
1 - Z_\epsilon = e^{-R_0 Z_\epsilon (1 - \nu - \epsilon)}.
\]

Proof: Note first that
\[
\frac{s_\infty}{s_0} = \frac{s_0 - (s_0 - s_\infty)}{s_0} = 1 - Z_\epsilon.
\]

Taking the limit \( t \to +\infty \) in the above Prop:
\[
\log \left( \frac{S_\infty}{S_0} \right) \left( = \log(1 - Z_\epsilon) \right) = -R_0 (r_\infty - r_0) = -R_0 Z_\epsilon (1 - \nu - \epsilon).
\]
\[ 1 - z_\varepsilon = e^{-R_0 z_\varepsilon (1 - v - \varepsilon)}. \]

★ If \( v = 0 \) and \( \varepsilon \to 0 \), then \( 1 - z_0 = e^{-R_0 z_0} \).
0 is always solution, but when \( R_0 > 1 \) there is a second positive solution in \((0, 1)\).

★ If \( v > 0 \) (vaccination), then 0 is the only solution if
\[ R_0 (1 - v) \leq 1 \iff v \geq 1 - \frac{1}{R_0} =: v_c \] (critical vaccination coverage).
Central limit theorem

★ Define:

\[ \eta_1^{1,N} = \sqrt{N}(s^{(N)}_t - s_t), \quad \eta_2^{2,N} = \sqrt{N}(i_t^{(N)} - i_t). \]

Assume that \((\eta_0^{1,N}, \eta_0^{2,N})\) converges in distribution to \((\eta_0^1, \eta_0^2)\) when \(N \to +\infty\).

★ Prop: Then for all \(T > 0\), \((\eta_1^{1,N}, \eta_2^{2,N})_{t \geq 0}\) converges in distribution in \(D([0, T], \mathbb{R}^2)\) to the Gaussian process characterized as the unique solution of

\[
\begin{align*}
d\eta^1_t &= -\lambda(i_t\eta^1_t + s_t\eta^2_t)\,dt - \sqrt{\lambda s_t i_t} \,dB^1_t, \\
d\eta^2_t &= \lambda(i_t\eta^1_t + s_t\eta^2_t)\,dt + \gamma\eta^2_t\,dt + \sqrt{\lambda s_t i_t} \,dB^1_t - \sqrt{\gamma i_t} \,dB^2_t,
\end{align*}
\]

where \(B^1\) and \(B^2\) are independent standard Brownian motions.
Course 1: Stochastic compartmental SIR model

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