

# Statistical estimation of the division rate of a size-structured population

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# 1 The problem

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- 2 Goldenshluger and Lepski's method

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- 4 Main results

## The informal problem and the PDE translation

- A cell grows.
- Depending on its size  $x$ , the cell has a certain chance to divide itself in 2 offsprings, ie 2 cells of size  $x/2$ .
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### Size-Structured Population Equation (finite time)

$$\begin{cases} \frac{\partial}{\partial t}(n(t, x)) + \kappa \frac{\partial}{\partial x}(g(x)n(t, x)) + B(x)n(t, x) = 4B(2x)n(t, 2x), \\ n(t, x=0) = 0, \quad t > 0 \\ n(0, x) = n_0(x), \quad x \geq 0. \end{cases}$$

- $n(t, x)$  the "amount" of cells with size  $x$  ( $\neq$  density),
- $g$  the "qualitative" growth rate of one cell: linear is  $g = 1 \dots$
- $B$  is the **division rate**, which depends on the size

## Asymptotics of the PDE

It can be shown (Perthame Ryzhik 2005 for instance) that

- $n(t, \cdot)$  grows exponentially fast ie  $I_t = \int n(t, x) dx$  asymptotically proportional to  $e^{\lambda t}$ ,
- the renormalized  $n(t, x)/I_t$  tends to a density  $N$ , which satisfies

### Size-Structured Population Equation (asymptotics)

$$\begin{cases} \kappa \frac{\partial}{\partial x} (g(x)N(x)) + \lambda N(x) = \mathcal{L}(BN)(x), \\ B(0)N(0) = 0, \quad \int N(x) dx = 1, \end{cases}$$

where

- for any real-valued function  $x \rightsquigarrow \varphi(x)$ ,  
 $\mathcal{L}(\varphi)(x) := 4\varphi(2x) - \varphi(x)$ .
- $\kappa = \lambda \frac{\int_{\mathbb{R}_+} xN(x) dx}{\int_{\mathbb{R}_+} g(x)N(x) dx}$ .

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- **Analytical** point of view:  $N_\epsilon$  is a noisy version of  $N$ , less regular than  $N$  (it is likely that no derivative exists) and  $\|N - N_\epsilon\|_2 \leq \epsilon$ . (see Perthame, Zubelli, etc)

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- **Statistical** point of view: we observe a  $n$ -sample  $X_1, \dots, X_n$  of iid variables with density  $N$ .

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$$K_h = \frac{1}{h} K(\cdot/h).$$

### Bias-Variance decomposition

$$\mathbb{E} \left( \left\| N - \hat{N}_h \right\|_2 \right) \leq \|N - K_h \star N\|_2 + \frac{1}{\sqrt{nh}} \|K\|_2,$$

where  $K_h \star N = \mathbb{E}(\hat{N}_h)$

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How to adaptively select  $h$ ? Recent work of Goldenshluger and Lepski (2009, 2010) Here just a "toy" version, but that's exactly what we needed.

## Selection of bandwidth

Set for any  $x$  and any  $h, h' > 0$ ,

$$\hat{N}_{h,h'}(x) := \frac{1}{n} \sum_{i=1}^n (K_h \star K_{h'})(x - X_i) = (K_h \star \hat{N}_{h'})(x),$$

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"estimator" of the bias term

$$A(h) := \sup_{h' \in \mathcal{H}} \left\{ \|\hat{N}_{h,h'} - \hat{N}_{h'}\|_2 - \frac{\chi}{\sqrt{nh'}} \|K\|_2 \right\}_+$$

where, given  $\varepsilon > 0$ ,  $\chi := (1 + \varepsilon)(1 + \|K\|_1)$ .

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$$\hat{h} := \arg \min_{h \in \mathcal{H}} \left\{ A(h) + \frac{\chi}{\sqrt{nh}} \|K\|_2 \right\} \quad \text{and} \quad \hat{N} := \hat{N}_{\hat{h}}.$$

# First result

## Oracle inequality

If  $\mathcal{H} = \{1/\ell \mid \ell = 1, \dots, \ell_{\max}\}$  and if  $\ell_{\max} = \delta n$ , if moreover  $\|N\|_{\infty} < \infty$ ,  
 then for any  $q \geq 1$ ,

$$\mathbb{E} \left( \|\hat{N} - N\|_2^{2q} \right) \leq \square_q \chi^{2q} \inf_{h \in \mathcal{H}} \left\{ \|K_h \star N - N\|_2^{2q} + \frac{\|K\|_2^{2q}}{(hn)^q} \right\} +$$

$$\square_{q, \varepsilon, \delta, \|K\|_2, \|K\|_1, \|N\|_{\infty}} \frac{1}{n^q}.$$

# Estimation of $D = \frac{\partial}{\partial x}(g(x)N(x))$

If  $K$  is differentiable,  $\int K = 1$  and  $\int |K'|^2 < \infty$ .

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$$\mathbb{E}(\|D - \hat{D}_h\|_2) \leq \|D - K_h \star D\|_2 + \frac{1}{\sqrt{nh^3}} \|g\|_\infty \|K'\|_2.$$

GL's trick

$$\hat{D}_{h,h'}(x) := \frac{1}{n} \sum_{i=1}^n g(X_i) (K_h \star K_{h'})'(x - X_i),$$

$$\tilde{A}(h) := \sup_{h' \in \tilde{\mathcal{H}}} \left\{ \|\hat{D}_{h,h'} - \hat{D}_{h'}\|_2 - \frac{\tilde{\chi}}{\sqrt{nh'^3}} \|g\|_\infty \|K'\|_2 \right\}_+,$$

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where, given  $\tilde{\varepsilon} > 0$ ,  $\tilde{\chi} := (1 + \tilde{\varepsilon})(1 + \|K\|_1)$ .

Finally, we estimate  $D$  by using  $\hat{D} := \hat{D}_{\tilde{h}}$  with

$$\tilde{h} := \operatorname{argmin}_{h \in \tilde{\mathcal{H}}} \left\{ \tilde{A}(h) + \frac{\tilde{\chi}}{\sqrt{nh^3}} \|g\|_\infty \|K'\|_2 \right\}.$$

## Result for the derivative $D$

### Oracle inequality for $D$

If  $\tilde{\mathcal{H}} = \{1/\ell \mid \ell = 1, \dots, \ell_{max}\}$  and if  $\ell_{max} = \sqrt{\delta' n}$ , if moreover  $\|N\|_\infty$  and  $\|g\|_\infty < \infty$ , then for any  $q \geq 1$ ,

$$\mathbb{E} \left( \|\hat{D} - D\|_2^{2q} \right) \leq \square_q \tilde{\chi}^{2q} \inf_{h \in \tilde{\mathcal{H}}} \left\{ \|K_h \star D - D\|_2^{2q} + \left[ \frac{\|g\|_\infty \|K'\|_2}{\sqrt{nh^3}} \right]^{2q} \right\} \\ + \square_{q, \tilde{\epsilon}, \delta', \|K'\|_2, \|K\|_1, \|K'\|_1, \|N\|_\infty, \|g\|_\infty} \frac{1}{n^q}.$$

## Estimation of $\lambda$ and $\kappa$

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### Assumption on $\hat{\lambda}$

There exist some  $q > 1$  such that

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Let  $c > 0$ ,

$$\hat{\kappa} = \hat{\lambda} \frac{\sum_{i=1}^n X_i}{\sum_{i=1}^n g(X_i) + c}.$$

## The inversion of $\mathcal{L}$

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$$0 = x_{0,k} < x_{1,k} < \dots < x_{i,k} := \frac{i}{k}T < \dots < x_{k,k} = T.$$

Set  $\varphi_{i,k} := \frac{k}{T} \int_{x_{i,k}}^{x_{i+1,k}} \varphi(x) dx$  for  $i = 0, \dots, k-1$ , and define by induction the sequence

$$H_{i,k}(\varphi) := \frac{1}{4} (H_{i/2,k}(\varphi) + \varphi_{i/2,k}) \text{ with } \begin{cases} H_0(\varphi) := \frac{1}{3} \varphi_{1,k}, \\ H_1(\varphi) := \frac{4}{21} \varphi_{0,k} + \frac{1}{7} \varphi_{1,k} \end{cases}$$

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for any sequence  $u_i, i = 1, 2, \dots$ ,

$$u_{i/2} := \begin{cases} u_{i/2} & \text{if } i \text{ is even} \\ \frac{1}{2} (u_{(i-1)/2} + u_{(i+1)/2}) & \text{otherwise.} \end{cases}$$

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Hence we are able to estimate  $H = BN$  by

$$\hat{H} = \mathcal{L}_k^{-1}(\hat{K}\hat{D} + \hat{\lambda}\hat{N}).$$

# Oracle inequality for the estimation of $H = BN$

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- $\left. + \left( \square_\alpha |\mathcal{L}(BN)|_{C^\alpha(T)} T^{\alpha+1/2} k^{-\alpha} \right)^q \right\} +$
- $\square \dots \frac{1}{n^{q/2}}.$

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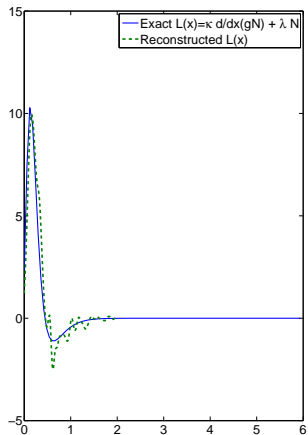
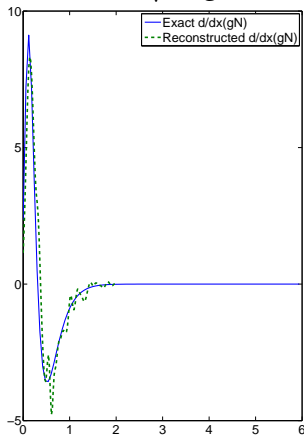
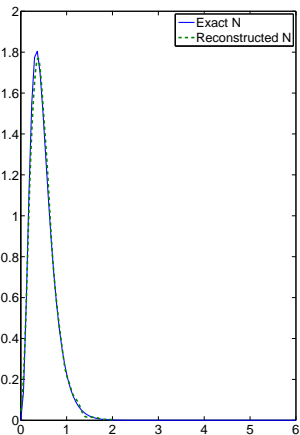
### Theorem

*If one knows a bound  $\alpha \geq s$ , one can choose a kernel  $K$  and a family of  $\mathcal{H}$  and  $\mathcal{H}'$  independent of  $s$  such that for any compact  $[a, b]$  of  $[0, T]$  (under technical assumptions),*

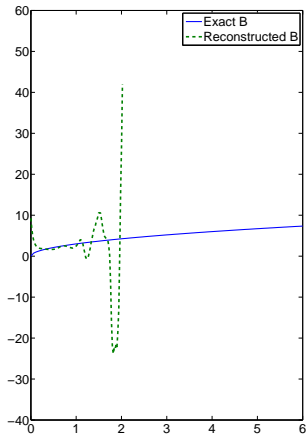
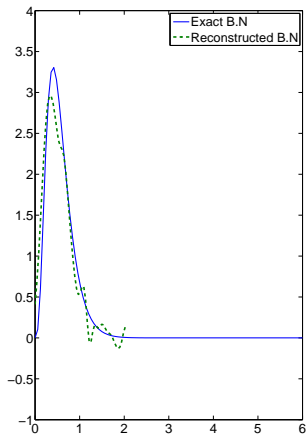
$$\mathbb{E} \left[ \left\| (\tilde{B} - B)1_{[a,b]} \right\|_2^q \right] = O \left( n^{-\frac{qs}{2s+3}} \right).$$

# Simulations

$n=5000$ , Gaussian kernel,  $B = 3\sqrt{x}$ ,  $g = 1$ .



# Simulations



## Concluding remarks

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- Probabilistic interpretation not used: evolution of one cell look like TCP window size, but the whole population (?)  $\rightsquigarrow$  chaos and not necessarily independence (work in progress of Hoffmann, Krell, Lepoutre ...)
- Calibration of GL's method not done, comparison with the L-curve method in analysis ( $\chi$  N step ?)