PINNs for structured population dynamics inference:
Application to oocyte dynamics in fish ovaries

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Inria

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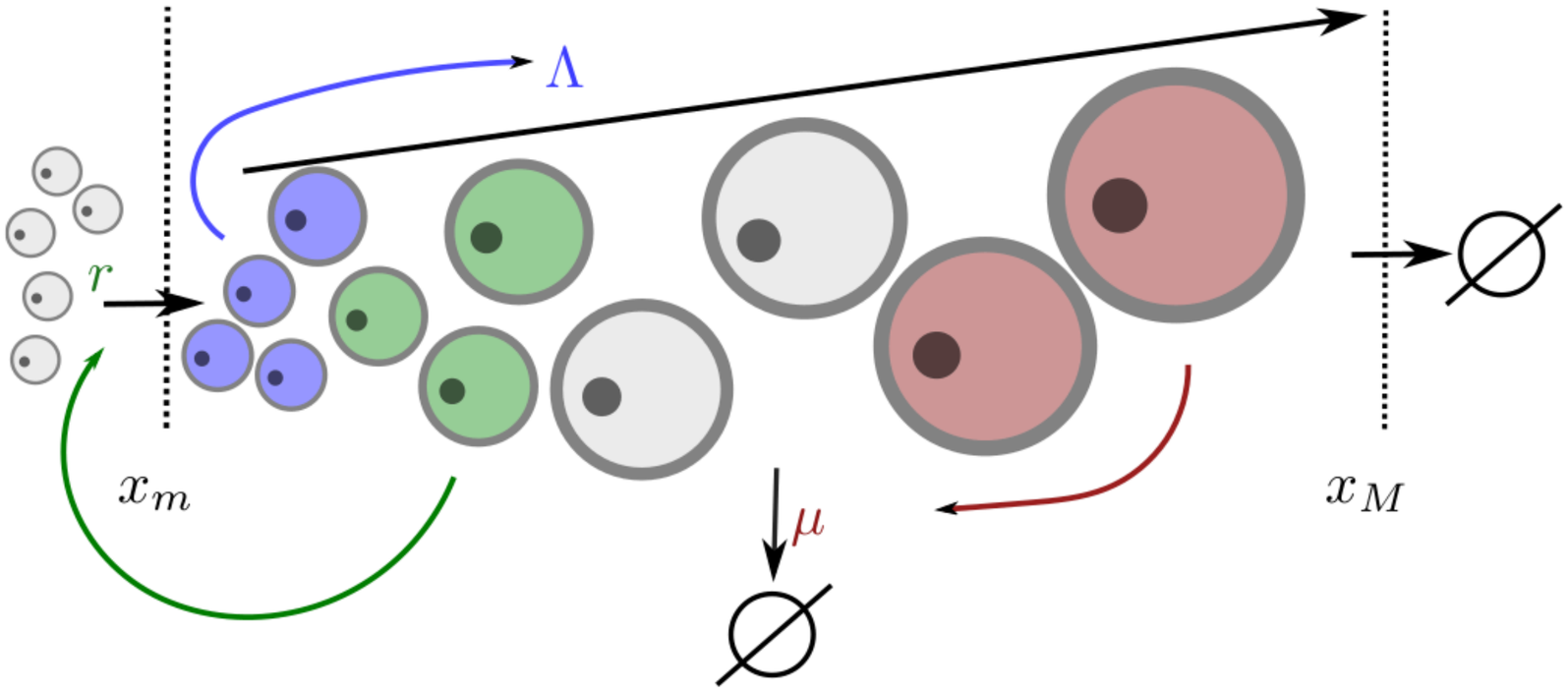
Contents

1 Size-structured population dynamics models

- Deterministic dynamics of a cell population structured by cell size x (maturity)
- Variable : Density of cells with respect to time and their size $\rho(t, x)$
- Demographic functions :
  - Recruitment (differentiation of precursor cells) at fixed size, at rate r
  - Growth at positive speed Λ
  - Death at rate μ
- Non local interaction terms (hormonal feedbacks, competition for ressources)



Size-structured population dynamics models

Quasilinear transport equation on cell size density :

$$
\begin{cases}
\partial_t \rho(t,x) + \partial_x(\Lambda(P(t),C(t),x)\rho(t,x)) + \mu(P(t),C(t),x)\rho(t,x) = 0 \\
\Lambda(P(t),C(t),x_r)\rho(t,x_r) = r(P(t),C(t)) \\
P(t) = \int_{x_r}^{x_m} \omega(x)\rho(t,x)\,dx, \\
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Size-structured population dynamics models

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- McKendrick (1925) : PDEs for size-structured population dynamics modeling
- Murphy (1983) : Non local interaction terms in demographic functions
- Calsina and Saldana (1995) : Well-posedness (characteristic method and fixed point argument)
- Well-posedness and long-time behaviour : Diekmann, Metz, Ackleh, Farkas, Magal, Ruan, Perthame,...

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Well-posedness and regularity :

- Under standard boundedness and smoothness assumptions on the demographic functions and interaction terms, **the model admits a unique global solution**.
- **The solution inherits the regularity of the demographic functions and initial density,** except possibly along the characteristic emanating from (0,0).

Clement F., **Fostier L.,** Yvinec R., Bifurcation analysis of a size-structured population model: Application to oocyte dynamics and ovarian cycle**,** *in SIAM Journal on Applied Dynamical System, 2025*

3 Size-structured population dynamics models : Inverse problem

Prior knowledge :

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qualitative knowledge on parameters
(monotonicity, bounds)

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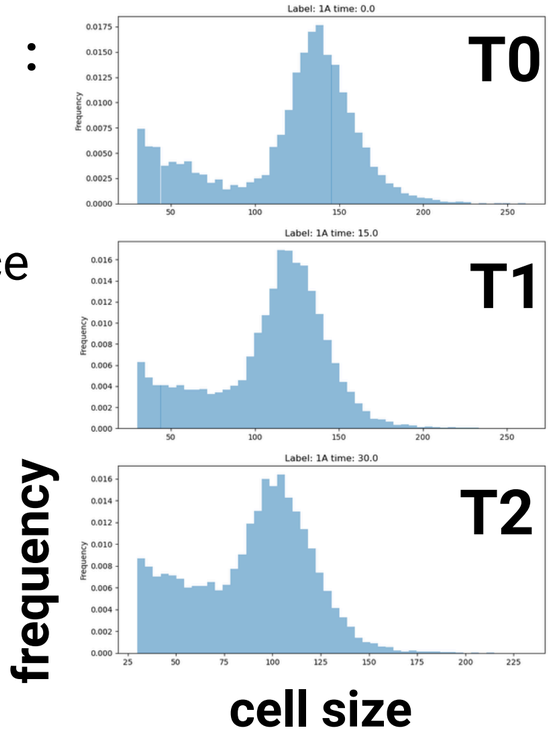
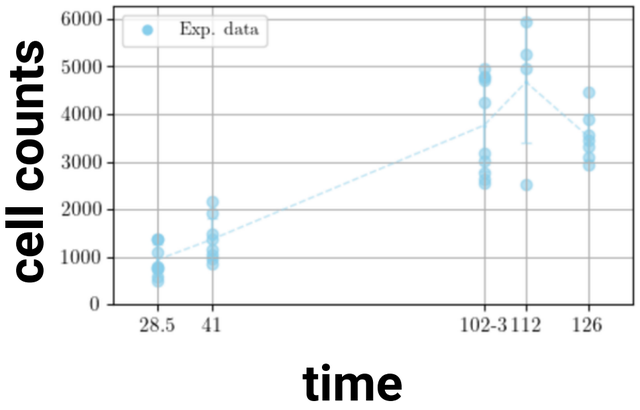
Observations (possibly normalized, partial, sparse in time) :

- Microscopic scale : cell size distributions
- Macroscopic scale : cell counts, counts of cells within specific size classes, hormonal measurements, resource levels,...

Microscopic scale



Macroscopic scale



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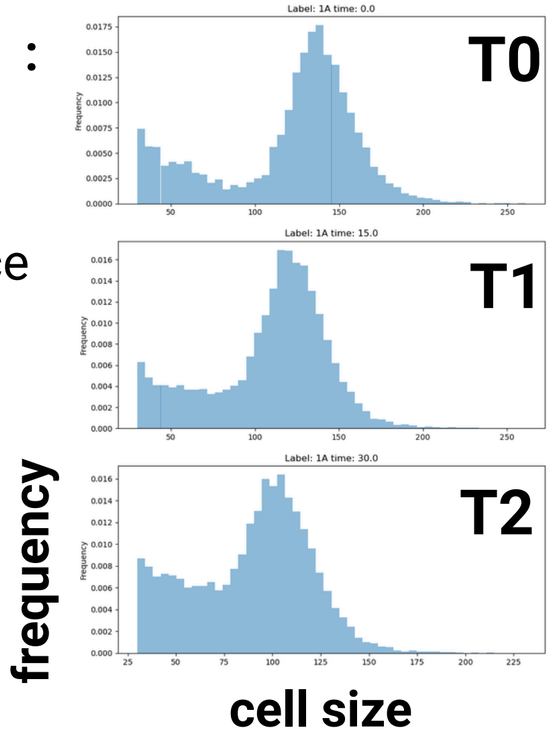
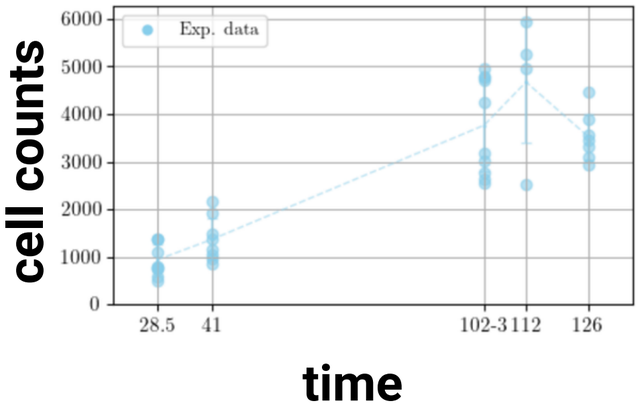
Goal :

- Infer unknown **demographic functions**
- Infer unknown **interactions dynamics**

Microscopic scale



Macroscopic scale



4 Size-structured population dynamics models : Inverse problem identifiability

Identifiability of inverse problems :

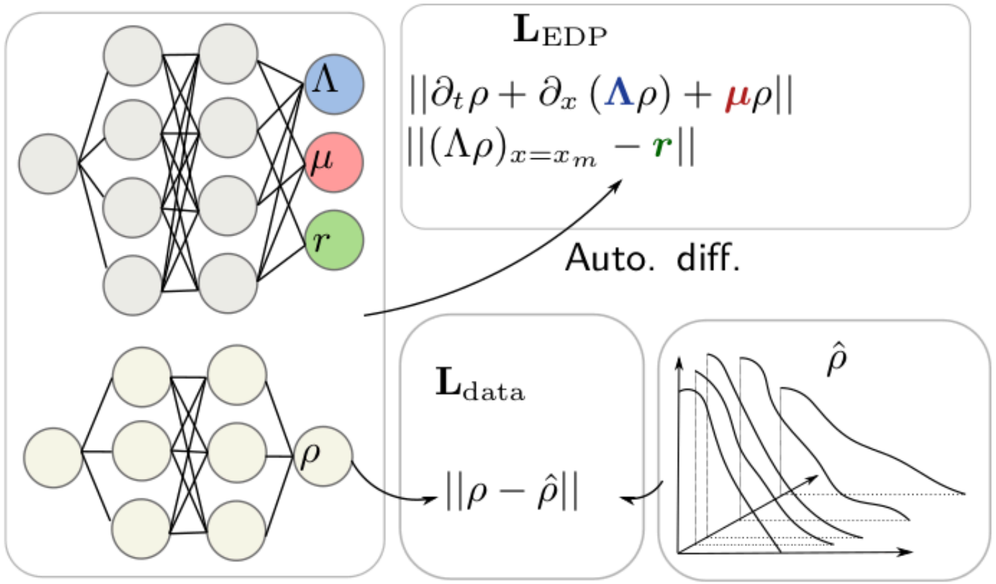
- **Problem-dependent** : depends on available data and prior biological knowledge
- **Structural identifiability** : with perfect (noise-free, infinite) data, what is identifiable?
- **Practical identifiability :** with real (noisy, limited) data, does the inference procedure converge?

Practical strategy :

- Check **structural identifiability** when possible
- Validate methodology using **synthetic datasets**

PINNs for data-driven inference of structured population PDE-ODE models

- Inference of **scalar and functional parameters** (recruitment, growth, death)
- **General framework** for structured population dynamics based on coupled PDE-ODE systems
- Handles non-local interactions (auxiliary-PINN methodology)
- Flexible integration of experimental data (multi-scale, partial, time-sparse observations)
- Efficient computational framework PyTorch



Related works :

- Raissi et al. (2017,2019) : PINNs for PDEs forward and inverse problems
- Largegren/Nardini et al. (2020,2026) : PINNs for equation learning with applications to biology (reaction-diffusion model)

PINNs for data-driven inference of structured population PDE-ODE models

Model reformulation to avoid explicit discretization of nonlocal interaction terms

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We define the auxiliary variable : $n(t,x) := \int_{x_r}^{x} \omega(y)\rho(t,y)\mathrm{d}y$

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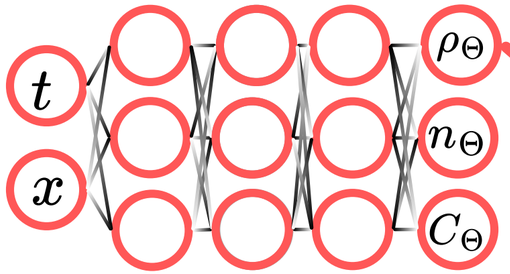
The fundamental theorem of calculus gives :

$$\begin{cases} \partial_t \rho(t,x) + \partial_x(\Lambda(n(t,x_m),C(t),x)\rho(t,x)) + \mu(n(t,x_m),C(t),x)\rho(t,x) = 0 \\ \partial_x n(t,x) = \omega(x)\rho(t,x) \\ \Lambda(C(t),x_r)\rho(t,x_r) = r(n(t,x_m),C(t)) \\ \frac{dC}{dt}(t) = F(C(t),n(t,x_m)) \\ \rho(0,x) = \rho_0(x), \quad n(t,x_r) = 0, \quad C(0) = C_0, \end{cases}$$

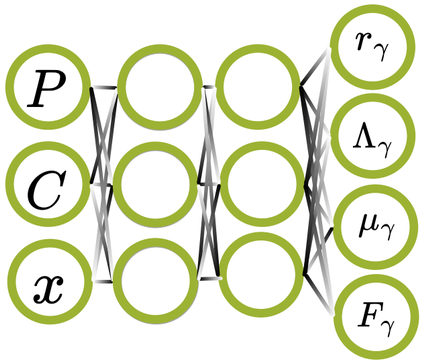
PINNs for data-driven inference of structured population PDE-ODE models

Neural networks (architecture include prior qualitative knowledge)

State variables



Parameters Θ



Biological functions

Parameters γ

Diff. Auto.

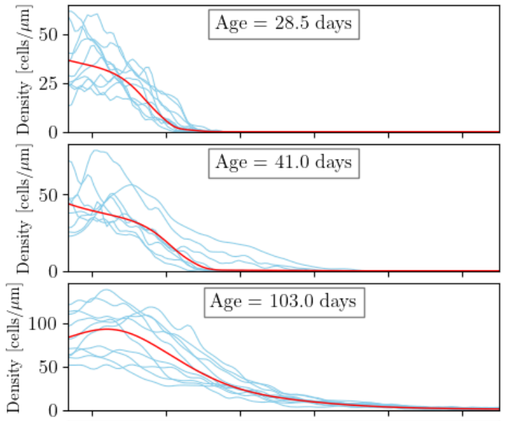
Loss function

Data error

$$||\rho_\Theta - \hat{\rho}_{data}||^2$$

+

Model error (residuals)



$$\underbrace{\|\partial_t \rho_\Theta + \partial_x\left(\Lambda_\gamma(n_\Theta(x_m), C_\Theta, \cdot)\,\rho_\Theta\right) + \mu_\gamma(n_\Theta(x_m), C_\Theta, \cdot)\,\rho_\Theta\|^2}_{\text{PDE residual}} +$$

$$\underbrace{\|\partial_x n_\Theta - \omega\rho_\Theta\|^2}_{\text{Auxiliary PDE residual}} \underbrace{\|C_\Theta{}' - F_\gamma(C_\Theta, n_\Theta(x_m))\,\|^2}_{\text{interaction term ODE residual}} +$$

$$\underbrace{\|\Lambda_\gamma(n_\Theta(x_m), C_\Theta, x_r)\,\rho_\Theta - r_\gamma(n_\Theta(x_m), C_\Theta)\|^2}_{\text{recruitment BC}}$$

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Regularisation terms (prior qualitative knowledge)

Optimization by backpropagation

PyTorch

PINNs for data-driven inference of structured population PDE-ODE models

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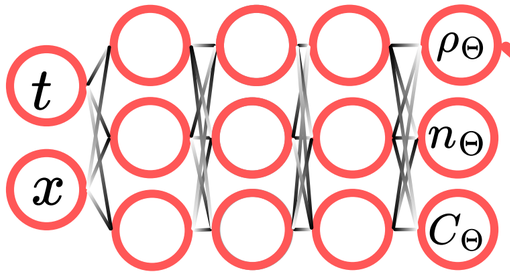

Parameters Θ

$r_\gamma(P, C; \gamma)$

$\Lambda_\gamma(P, C, x; \gamma)$

$\mu_\gamma(P, C; \gamma)$

$F_\gamma(P, C, x; \gamma)$

Biological functions

Parameters γ

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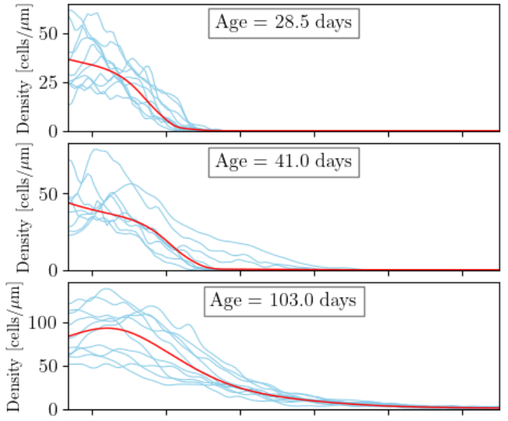

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PINNs for data-driven inference of structured population PDE-ODE models

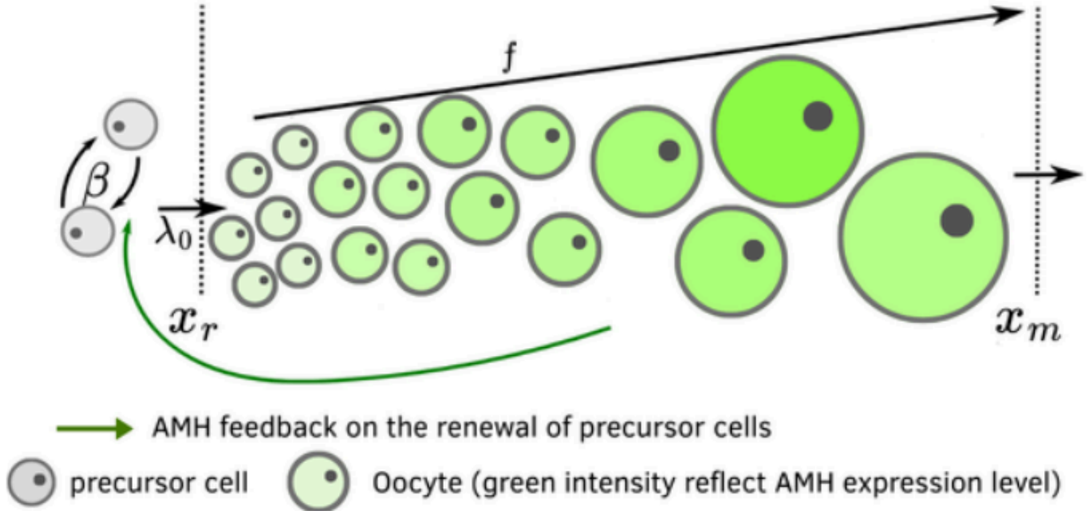
PINN-based inference pipeline :

1. Learn functional parameters using neural network representations (NP-PINN)
2. Parametrization : fit interpretable functional forms (manual design or model selection procedure)
3. Estimate the parameters of the functional forms (P-PINN)

Why parametric form ?

- **Interpretability :** recover a compact “mecanistic” model
- **Predictability :** Facilitate model exploration and sensitivity analysis, ...
- **Variability :** First step towards quantifying interindividual variability

Data-driven inference of oocyte dynamics in fish ovaries



- Oocyte grows from $x_r = 30\mu m$ to $x_m = 150\mu m$ at a size-dependant speed $\Lambda(x)$
- AMH (hormonal signal) is produced by the oocyte population :
  ω_{AMH} is the size-dependant oocyte AMH expression level (a priori known).
- Precursor cells self-renew at AMH-dependant rate $\beta(P(t))$ and differentiate into oocyte at rate λ_0

$$\begin{cases} \partial_t \rho(t,x) + \partial_x(\Lambda(x)\rho(t,x)) = 0,\ t > t_0,\ x \in (x_r, x_m) \\ \Lambda(x_r)\rho(t,x_r) = \lambda_0 S(t),\ t > t_0 \\ P(t) = \int_{x_r}^{x_m} \omega_{AMH}(x)\rho(t,x)\,dx,\ t > t_0 \\ \frac{dS}{dt}(t) = (\beta(P(t)) - \lambda_0)S(t),\ t > t_0 \end{cases}$$

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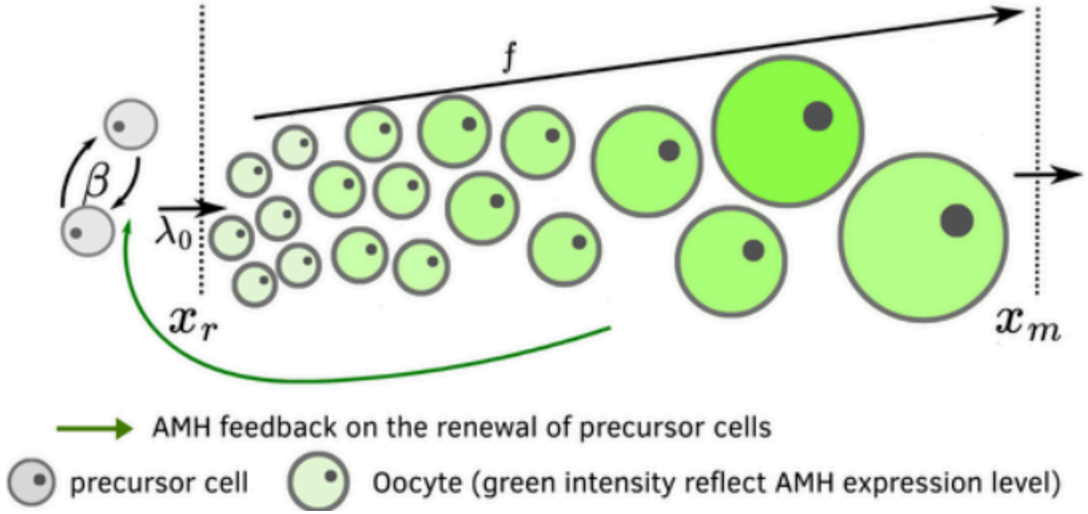

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Structural identifiability

Model :

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Perfect data : $(t,x) \mapsto \rho(t,x),\ \forall t > t_0, x \in (x_r, x_m)$

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Perfect data : $(t,x) \mapsto \rho(t,x),\ \forall t > t_0, x \in (x_r, x_m)$

Explicit reconstruction of biological functions of interest :

$$C(t) = f(x_m)\rho(t,x_m) + \frac{d}{dt}\int_{x_r}^{x_m} \rho(t,x)dx$$

$$\Lambda(x) = \frac{C(t) - \frac{d}{dt}\int_{x_r}^{x} \rho(t,y)dy}{\rho(t,x)}$$

$$\alpha(P(t)) = \frac{C'(t)}{C(t)}$$

Data-driven inference of oocyte dynamics in fish ovaries

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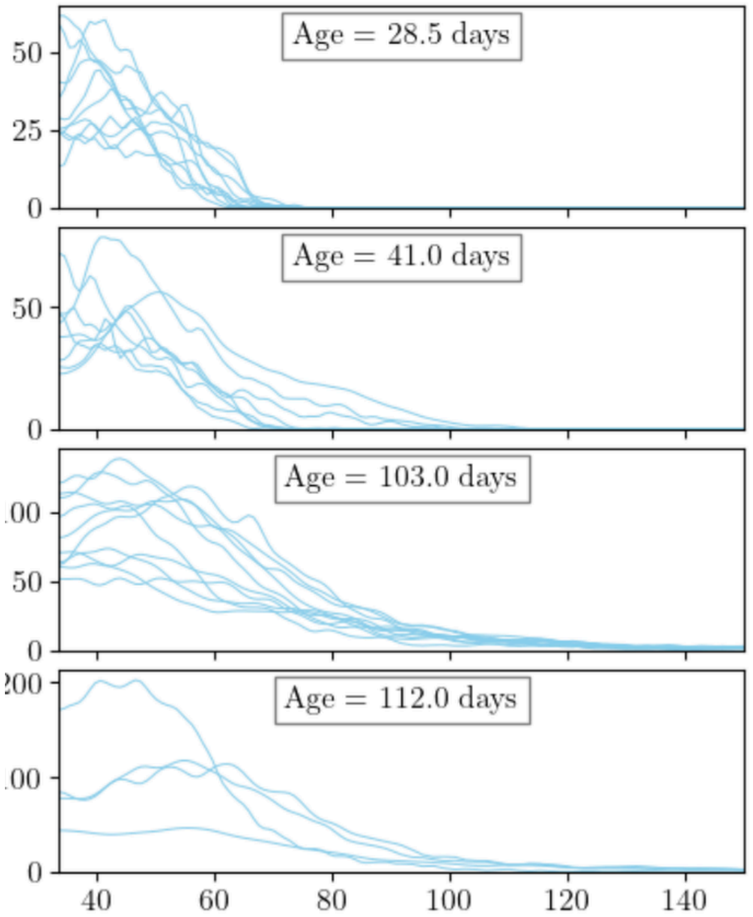
Practical identifiability

Experimental data (destructive measurements, reconstruction of a pseudo-time series of 4 points)

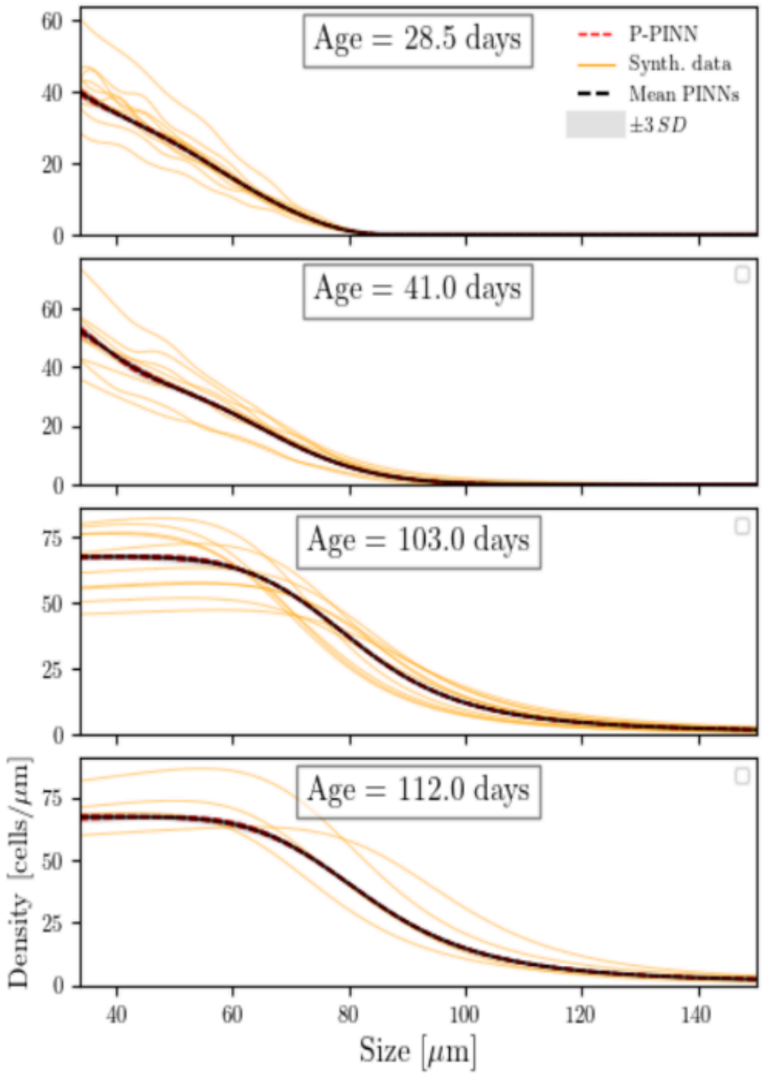


We generate a synthetic dataset

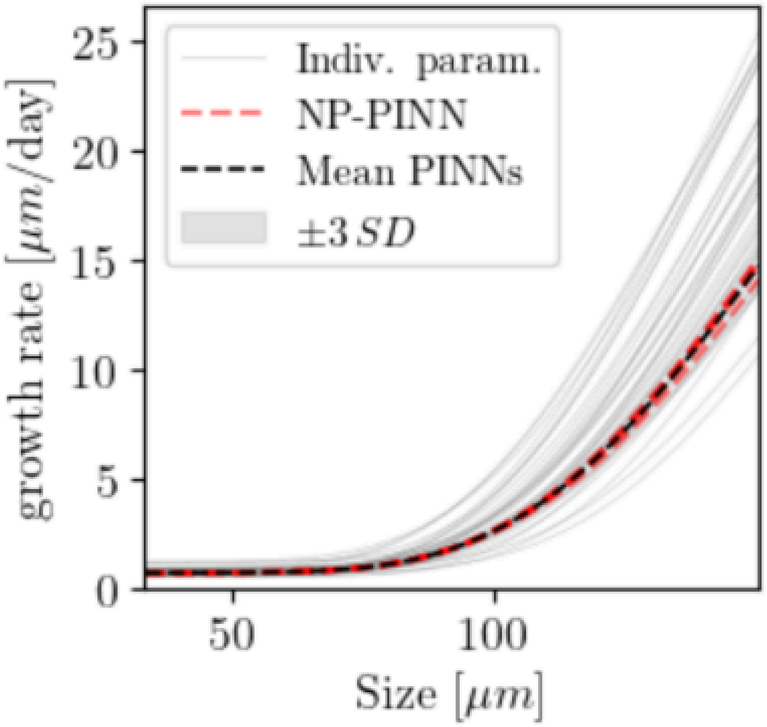
and assess the quality of the biological functions recovery

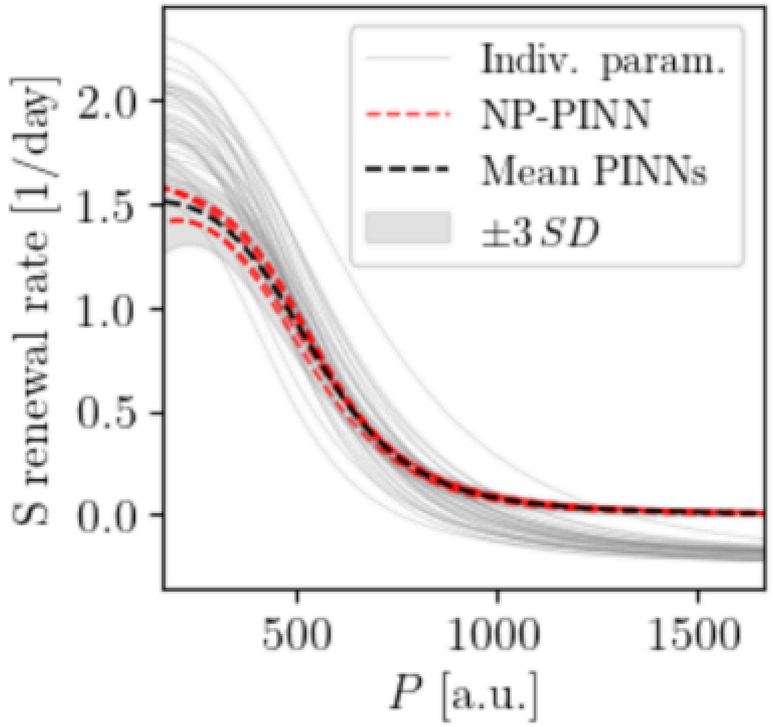
Data-driven inference of oocyte dynamics in fish ovaries

Synthetic dataset :



Practical identifiability :

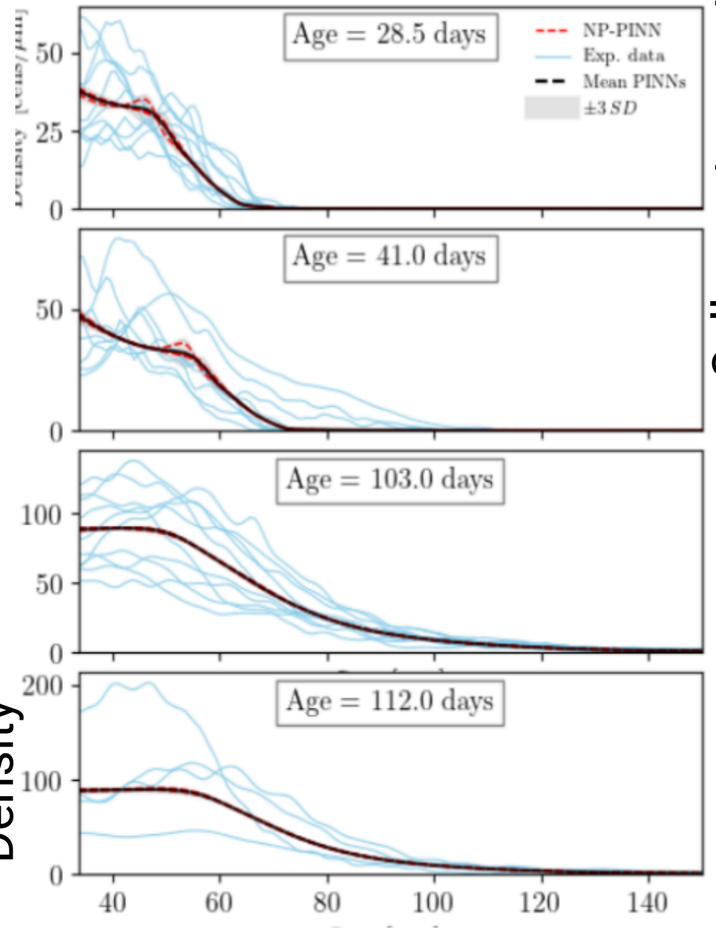




Main difficulty : Destructive measurements + interindividual variability

Data-driven inference of oocyte dynamics in fish ovaries

NP-PINN vs data



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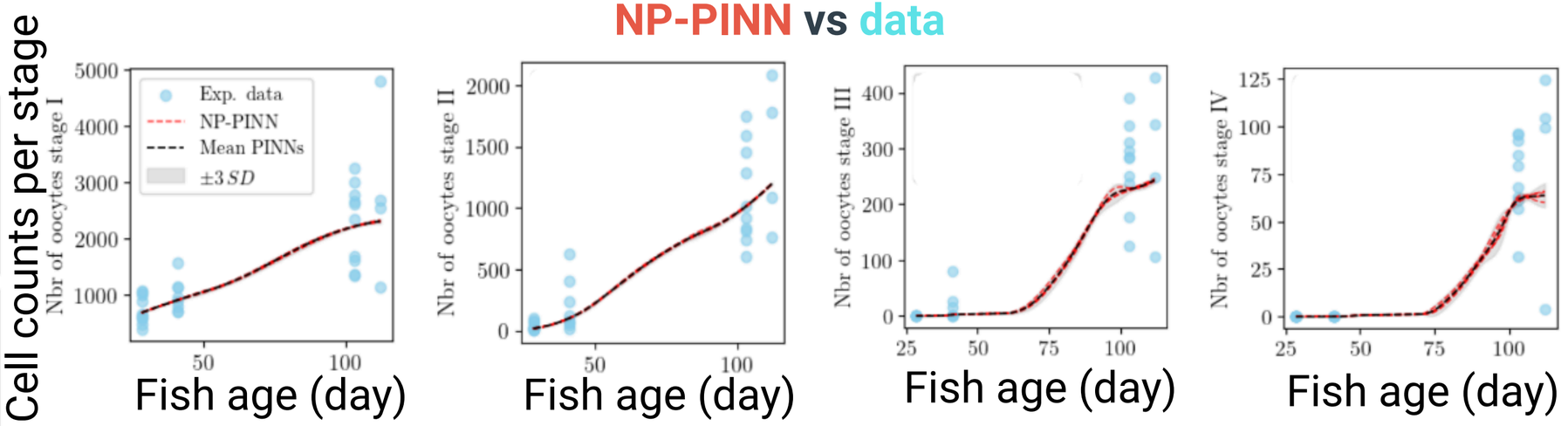
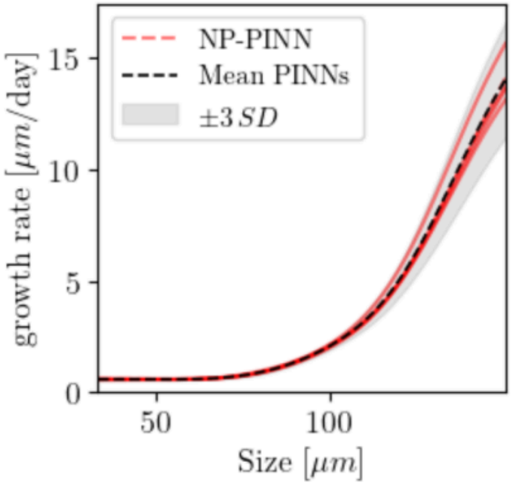
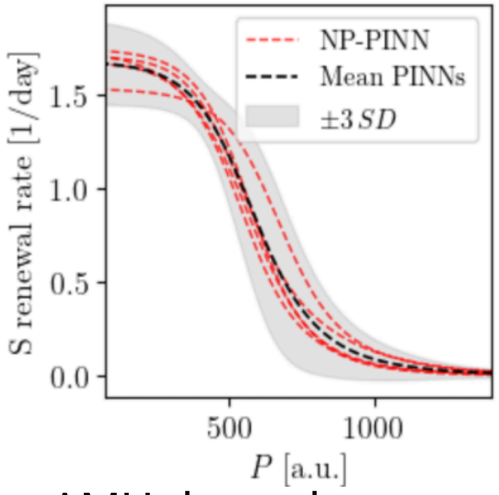


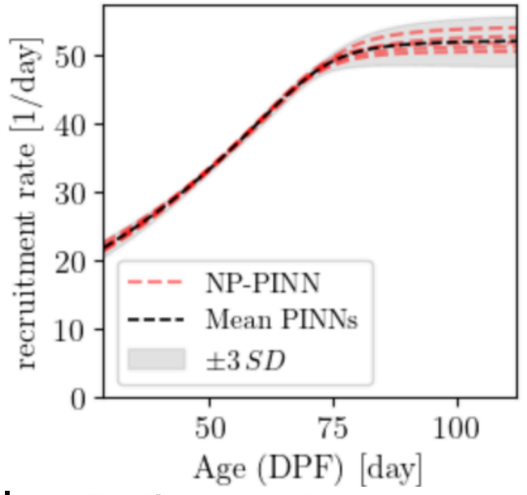
Non parametric inference of biological functions



Cell size-dependant growth rate



AMH-dependant renewal rate of precursor cells



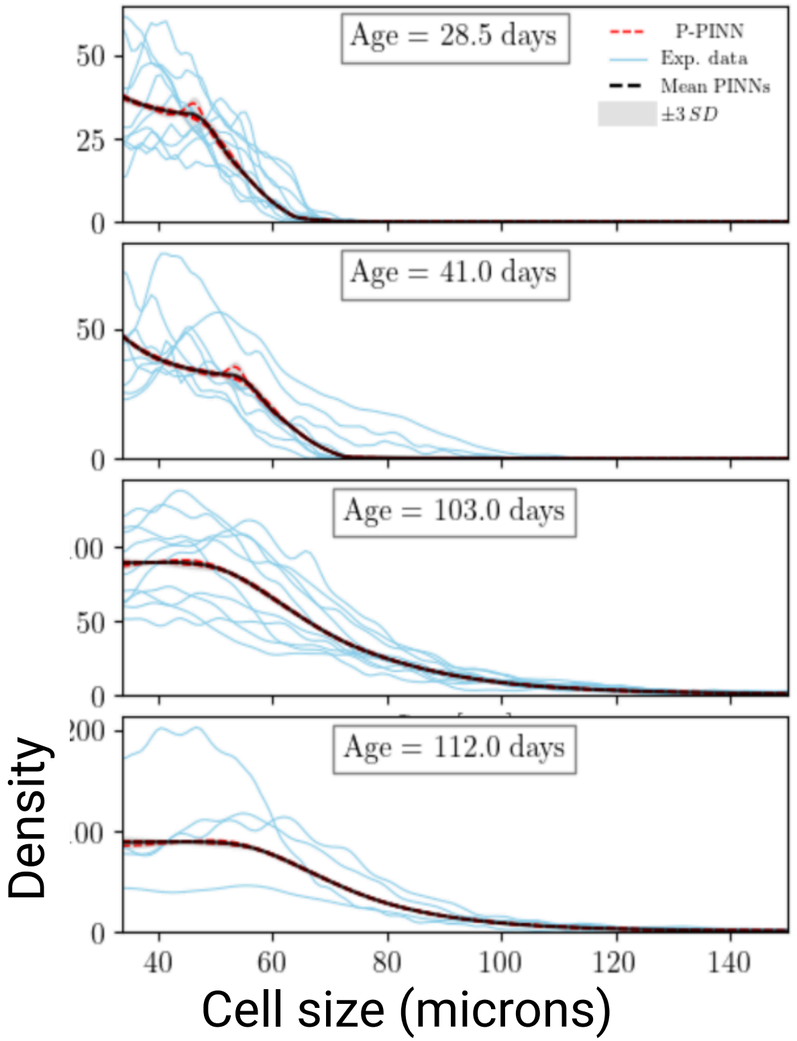
Daily recruitment rate of new oocytes

Data-driven inference of oocyte dynamics in fish ovaries

- **Gompertz growth rate** $\Lambda(x) = f_0 + Ae^{-Be^{-C\frac{x-x_r}{x_m-x_r}}}$
- **Sigmoidal AMH-dependant renewal rate** $\alpha(P) = \alpha_{min} + \frac{\alpha_{max} - \alpha_{min}}{1 + \left(\frac{P}{P_m}\right)^k}$

Data-driven inference of oocyte dynamics in fish ovaries

P-PINN vs data



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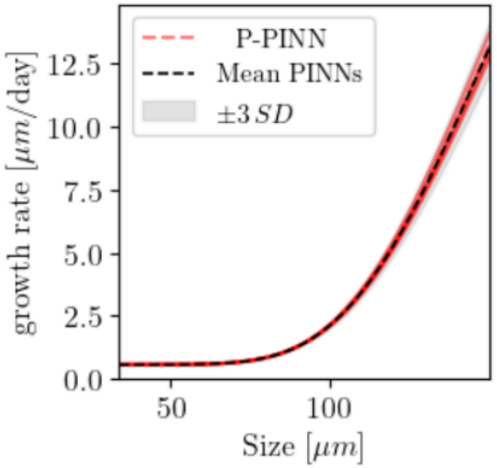
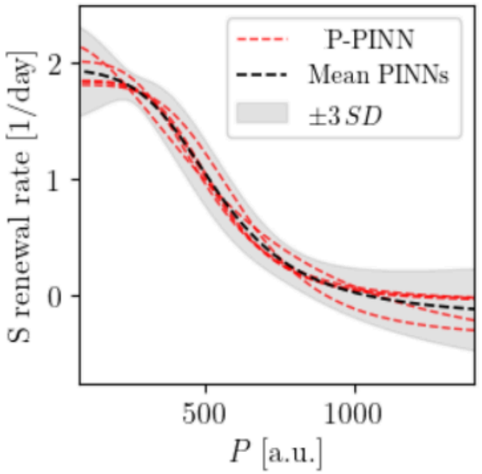
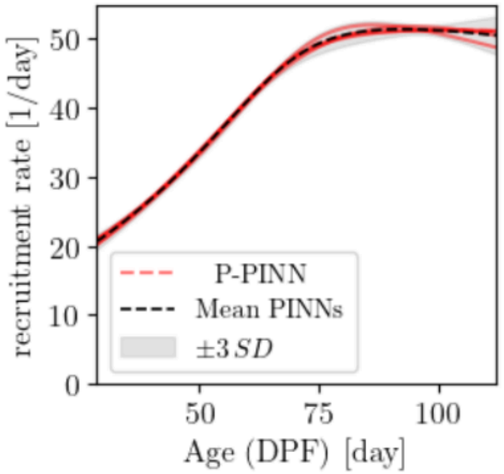
Parametric inference of biological functions







Oocyte growth rate (f)		AMH-dependent net renewal rate (α)	
Parameter	Estimate	Parameter	Estimate
A	35.85 ± 0.60	$\alpha_{\min}$	-0.22 ± 0.22
B	13.36 ± 0.18	$\alpha_{\max}$	1.94 ± 0.14
C	2.54 ± 0.03	P_{m}	553.8 ± 44.8
f_0	0.57 ± 0.002	k	3.95 ± 0.98

Data-driven inference of oocyte dynamics in fish ovaries

- **Gompertz growth rate** $\Lambda(x) = f_0 + Ae^{-Be^{-C\frac{x-x_r}{x_m-x_r}}}$

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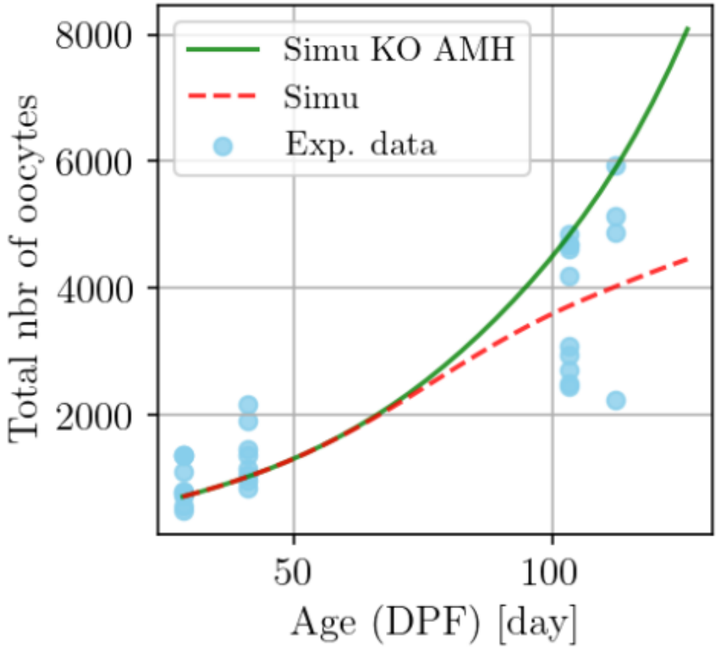
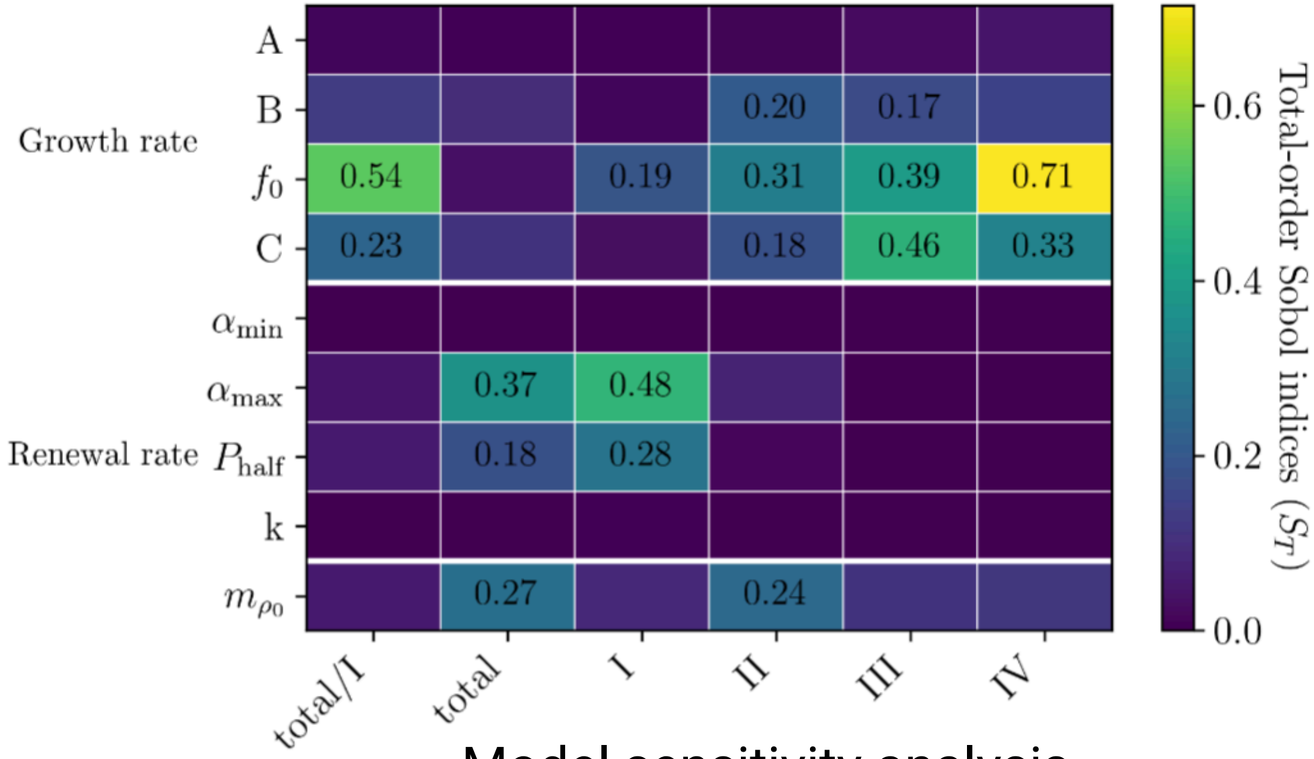
Model exploration



Simulation of AMH invalidation
in agreement with AMH invalidation
experimental studies

Interindividual variability explaination



Model sensitivity analysis

Perspective : PINNs for equation learning

Inference of compact (interpretable) data-driven models :

- Automate the parametric model inference (regression techniques + model selection)
- Uncertainty quantification
- **Populationnal approach (mixed-effect model) to quantify interindividual variability**

Related works :

- Mechanistic dynamic modelling of biological systems: The road ahead, Julio R. Banga and Alejandro F. Villaverde, *Current Opinion in Systems Biology*, 2025
- Learning structured population models from data with WSINDy, Rainey Lyons , Vanja Dukic, David M. Bortz, *Plos Computational Biology*, 2025
- Learning functional components of PDEs from data using neural networks, Torkel E Loman et al., Preprint, 2026

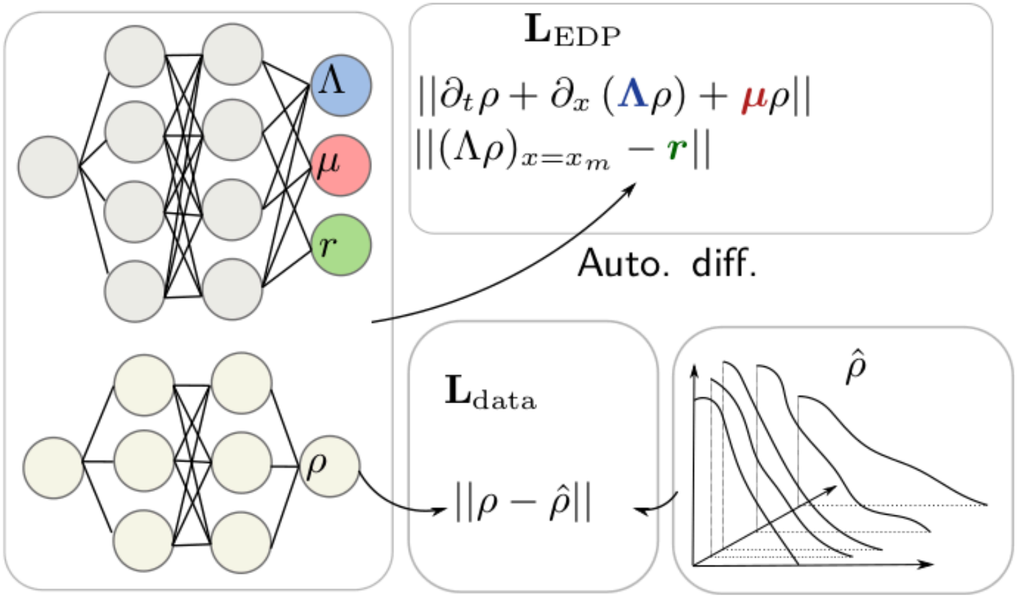
Perspective : PINNs for PDEs - mixed-effects models

Données biologiques :

- Parcimonieuses en temps
- Populationnelles (plusieurs individus θ_i)
- Multi-conditions (plusieurs environnements)

Effets mixtes :

- Modèle populationnel $\theta_i = \theta_\mu + \eta_i,\ \eta_i \sim \mathcal{N}(0, \theta_\sigma)$
- Quantifie la variabilité interindividuelle
- Améliore l'identifiabilité vs fits individuels
- Très peu utilisé pour EDP (Grenier et al. 2014,2018, Collin 2025)



PINNs pour modèle EDP-EDO à effets mixtes :

- Option A : PINN paramétrique comme surrogate pour SAEM
- Option B : SAEM - PINN intégré (optimisation simultanée)
- Effets mixtes paramétriques scalaires puis fonctionnels

Inférence de système dynamique (EDO) guidée par les données

Motivation :

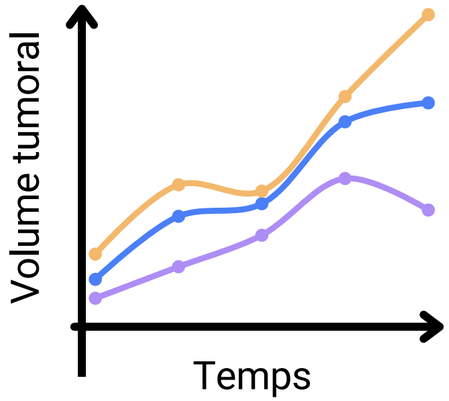
- Inférence d'une loi d'évolution **compacte et interprétable** d'un système dynamique **à partir de données**
- Améliorer l'**expressivité** des méthodes existantes (SINDy)

Méthode :

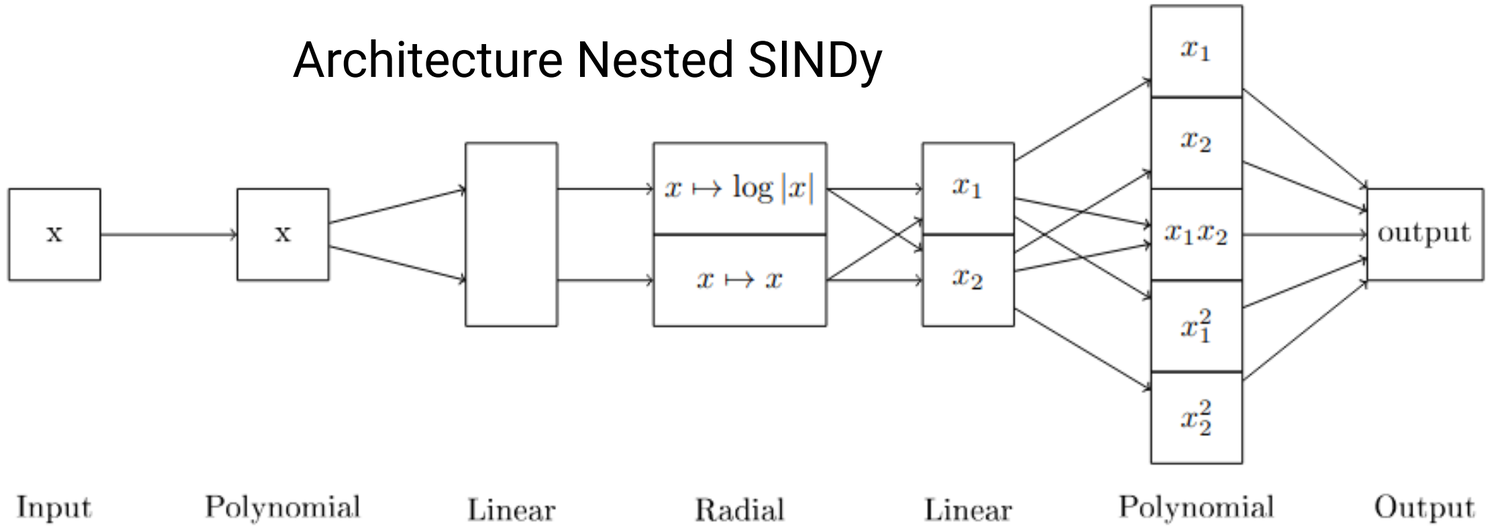
- Inférence parcimonieuse de la loi d'évolution, composition de combinaisons linéaires de fonctions
- Architecture et algorithme d'optimisation inspirés des réseaux de neurones

Applications biologie/santé:

Croissance tumorale



Architecture Nested SINDy



Fiorini C., Flint C., Fostier L., Franck E., Hashemi R., Michel-Dansac V., Tenachi W.,
Generalizing the SINDy approach with nested neural networks, *in ESAIM: Proceedings and surveys, 2025*

Projet BOUM SMAI avec C. Weckel : Inférence de signalisation intracellulaire (CRN) par des méthodes de régression parcimonieuse

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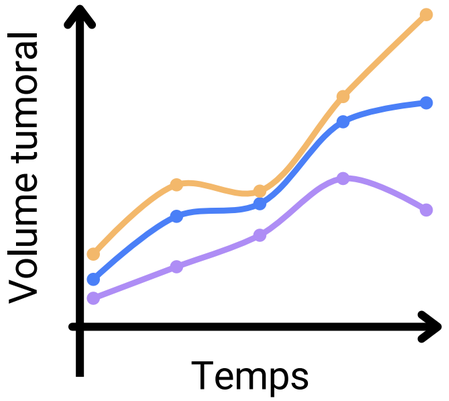

Apprentissage d'une fonction de croissance interprétable (Gompertz)

Epoch	f_θ	MSE on $[0,3]$	MSE on $[0,5]$	pruned parameters
50	expression too long to display	1.50×10^{-1}	3.83×10^{-1}	4
150	expression too long to display	5.18×10^{-2}	1.78×10^{-1}	5
300	expression too long to display	5.31×10^{-2}	1.22×10^{-1}	7
1000	$1.19x^2 - 2.03x(0.39x + 1.24\log(1.16\lvert x\rvert))$	9.17×10^{-2}	1.97×10^{-1}	9
1500	$-0.94x(0.46x + 1.55\log(0.77\lvert x\rvert))$	2.17×10^{-1}	3.83×10^{-1}	10
1900	$-1.98x\log(\lvert x\rvert))$	1×10^{-2}	1×10^{-2}	11

Fiorini C., Flint C., Fostier L., Franck E., Hashemi R., Michel-Dansac V., Tenachi W.,
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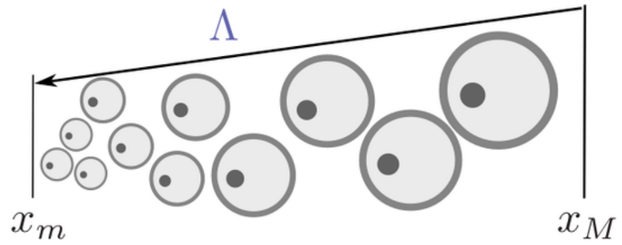
Inférence de modèles EDP-EDO de populations structurées

Travaux en cours avec **C. Audebert et H. Soula** Inférence PINNs de la dynamique des adipocytes pendant un protocole de restriction alimentaire

Modèle : Décroissance (lipolyse) taille-dépendante des adipocytes



$$\begin{cases} \partial_t \rho(t,x) - \partial_x \left(\Lambda(x)\rho(t,x)\right) = 0, \\ \Lambda(x_M)\rho(t,x_M) = 0, \\ \Lambda(x_m) = 0 \end{cases}$$

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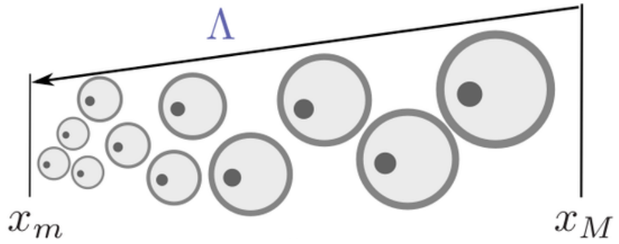

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Données :

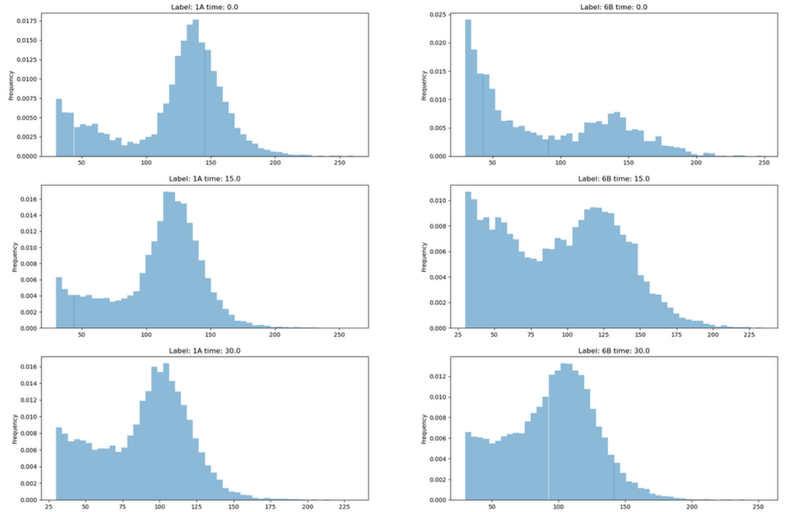
- 10 individus (rats)
- 3 points de temps par individu
- Distribution en taille normalisée et partielle

$$\frac{\rho(t,x)}{\int_{x_{obs}}^{x_M} \rho(t,y)dy}, \; x \in [x_{obs}; x_M]$$

Jour 0

Jour 15

Jour 30



Individu 1 **Individu 2** **...**

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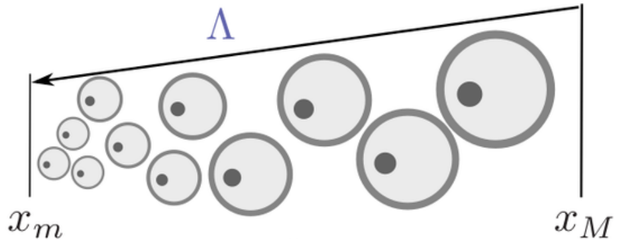

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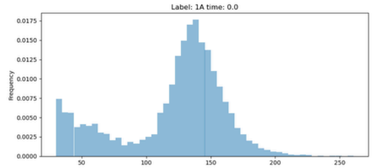
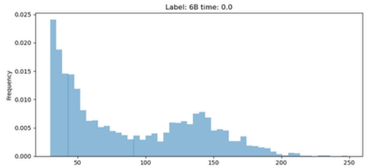
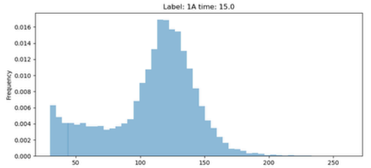
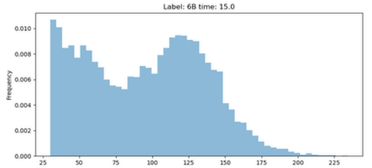


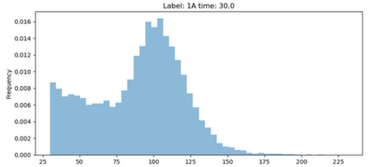


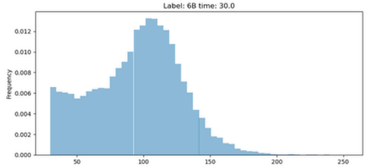
Jour 15





Jour 30



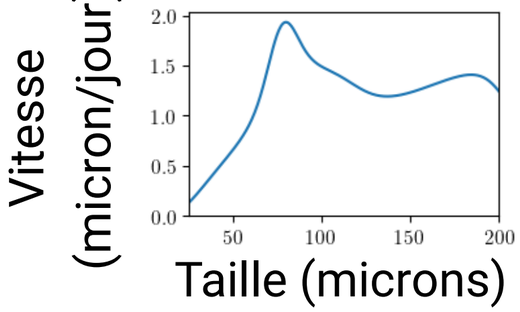


...

Résultats :

Inférence individuelle pour chacun des 10 rats de la vitesse de décroissance des adipocytes taille-dépendante

Individu 1



Individu 2