



Comparative dynamics of female germ cell populations : insight from imaging and multiscale modeling

Frédérique Clément, Romain Yvinec

► To cite this version:

Frédérique Clément, Romain Yvinec. Comparative dynamics of female germ cell populations : insight from imaging and multiscale modeling. Journées INRAE-INRIA 2023, Jul 2023, Nancy, France. hal-04194047

HAL Id: hal-04194047

<https://hal.inrae.fr/hal-04194047>

Submitted on 1 Sep 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

Comparative dynamics of female germ cell populations : insight from imaging and multiscale modeling

Frédérique Clément, Romain Yvinec

Journées INRAE-INRIA, 04-05 Juillet 2023

Outline

Collaborative background

Biological background

Available and future data

Modeling questions and approaches

Collaborative background

- EPC CNRS-INRAE-INRIA MUSCA

MULTiSCAle population dynamics for physiological systems

CRI Saclay – MaiAGE – PRC

- Projet GinFiz ANSES 2020

*Gonadal aromatase inhibition and other toxicity pathways leading to Fecundity Inhibition in Zebrafish:
from initiating events to population impacts*

collaboration INERIS (Rémy Beaudouin) + Laboratoire de Physiologie et Génomique des Poissons (LPGP,
Violette Thermes)

- Projet IMMO Digit-Bio INRAE 2021

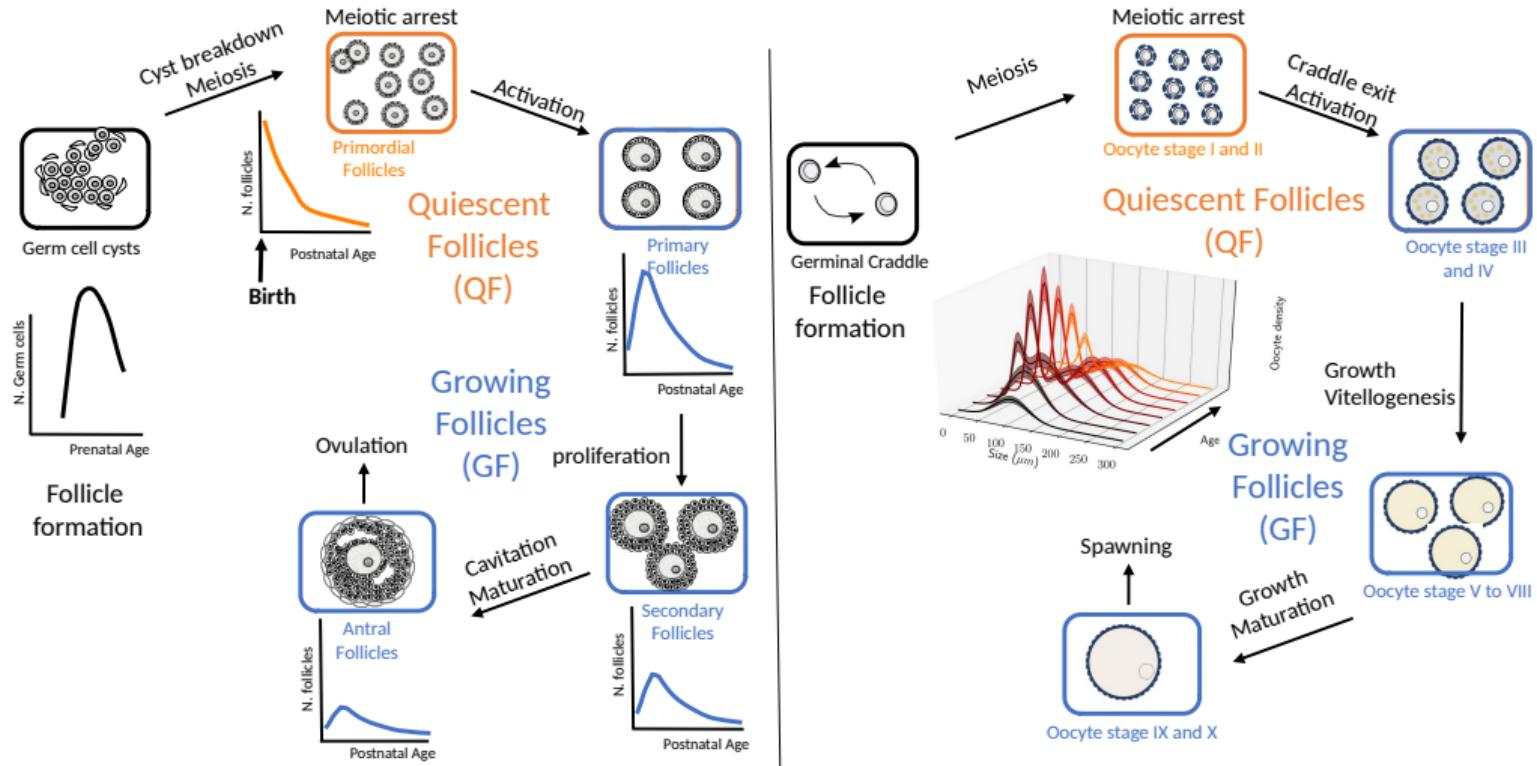
Imagerie et modélisation multi-échelles pour la compréhension de la dynamique ovarienne chez le poisson
collaboration LPGP

- AAPG ANR CES 45 OVOPAUSE 2022

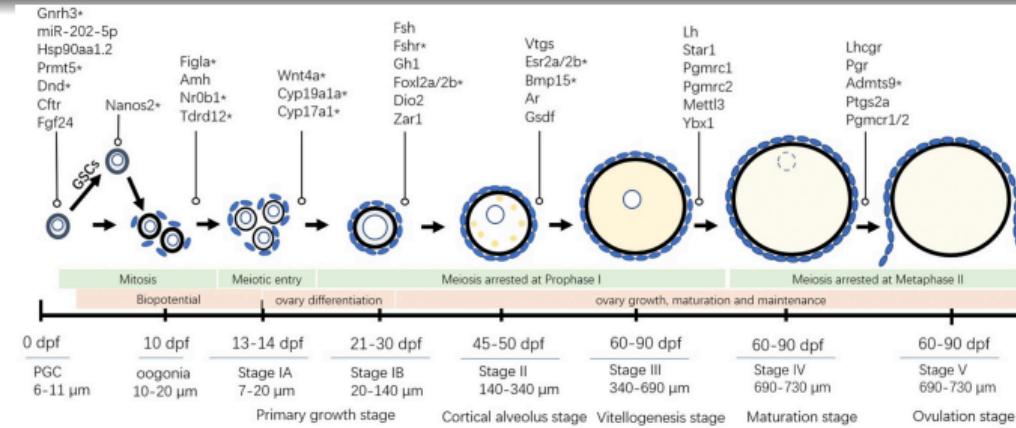
*Dynamics and regulation of female germ cell populations: understanding aging through population
dynamics models*

collaboration LPGP + INSERM

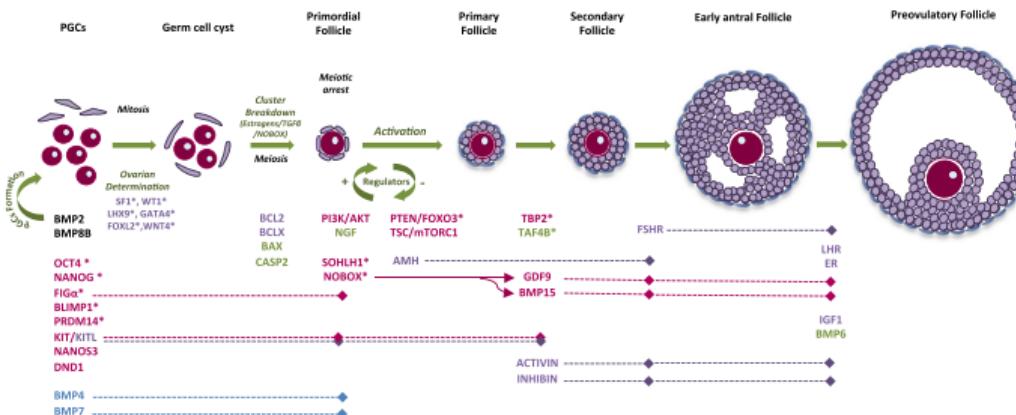
Comparative vertebrate oogenesis (1)



Comparative vertebrate oogenesis (2)



Li & Ge Mol. Cell. Endocrinol. 2020



Sánchez & Smith Acta Bioch. Biophys. 2012

Main questions and related outcomes

Population scale

- Kinetics of oocyte pool exhaustion / intensity of oocyte pool renewal
- Shaping of the oocyte (size/maturation) distribution
- Contribution of direct and indirect interactions within the oocyte population
Management of oocyte resources / Driving of ovarian cyclicity

Oocyte/follicle scale

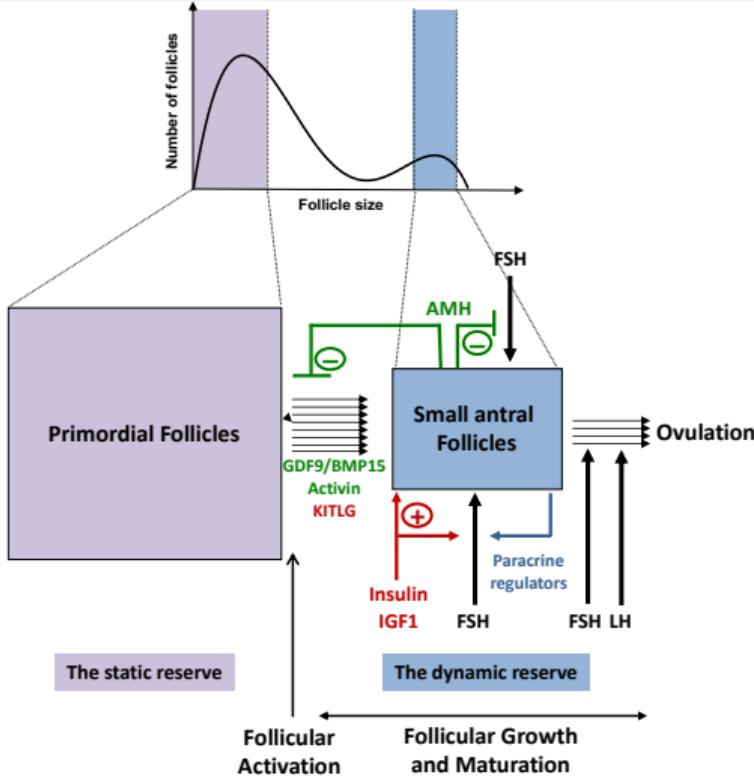
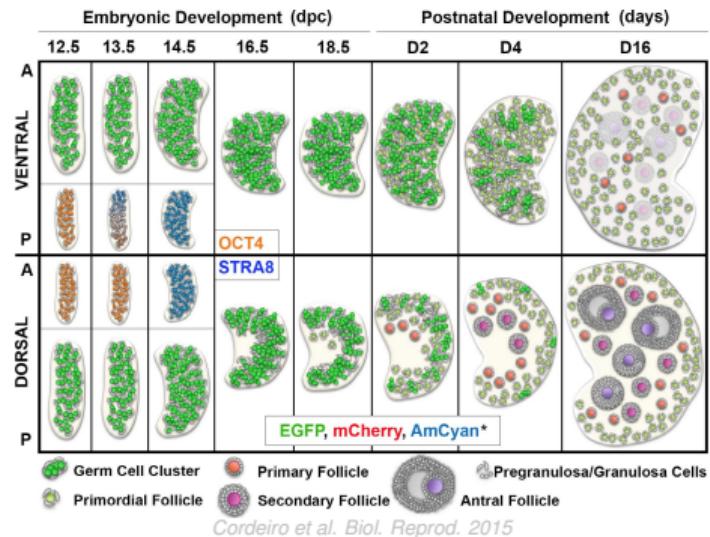
- Coupled dynamics between germ cells and somatic cells
- Mechanisms underlying the proper sequence of morphogenetic events

Preserving the ovarian resources

- Ovarian aging
- Reproductive fitness

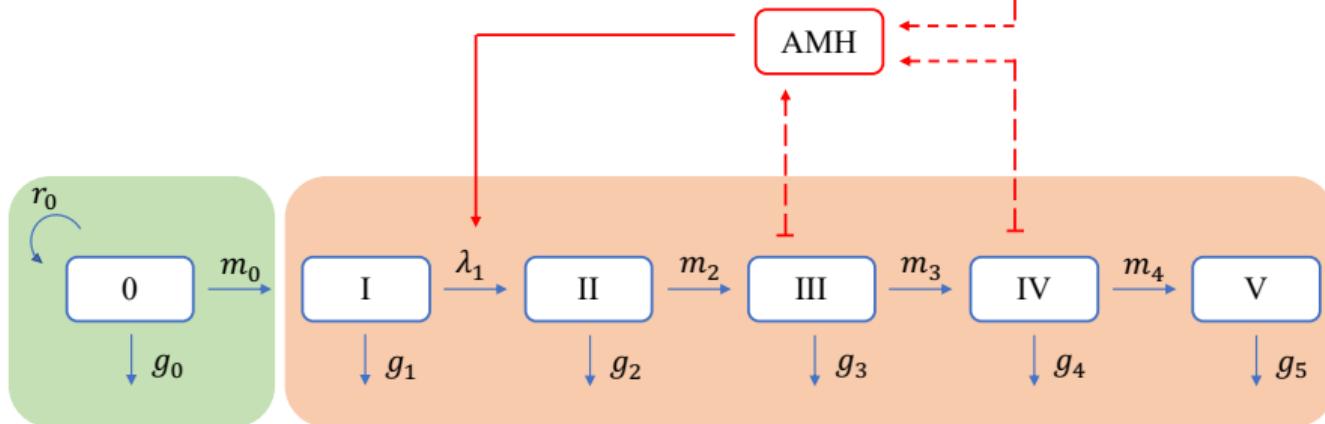
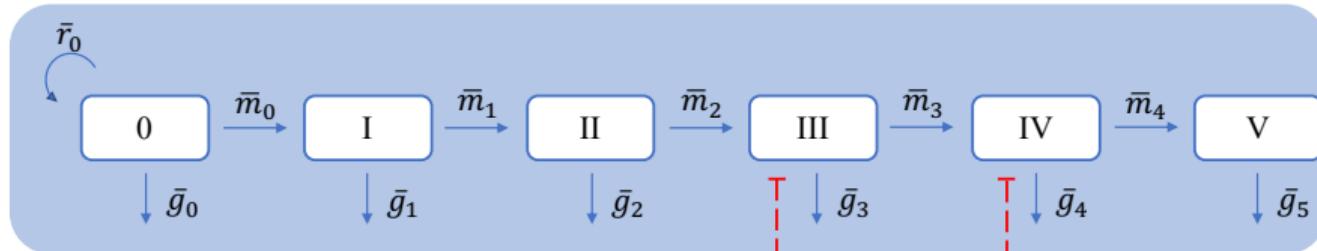
Knowledge driven modeling approaches (Mammals)

Embedding cell biology/developmental biology/endocrine information



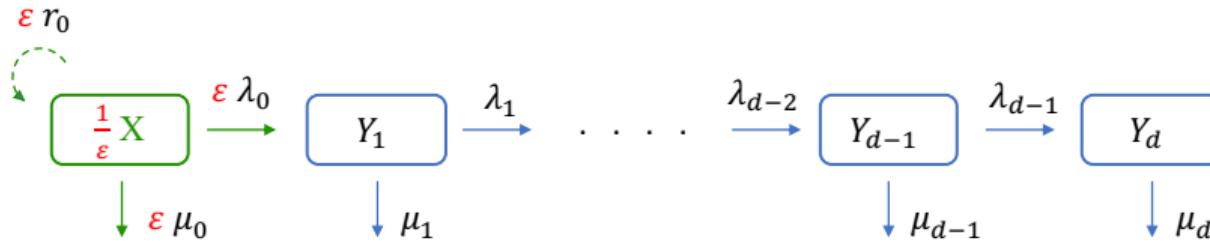
Knowledge driven modeling approaches (Mammals)

Embedding cell biology/developmental biology/endocrine information



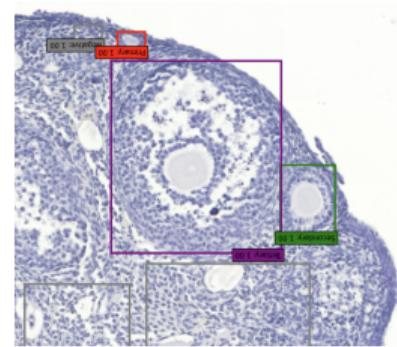
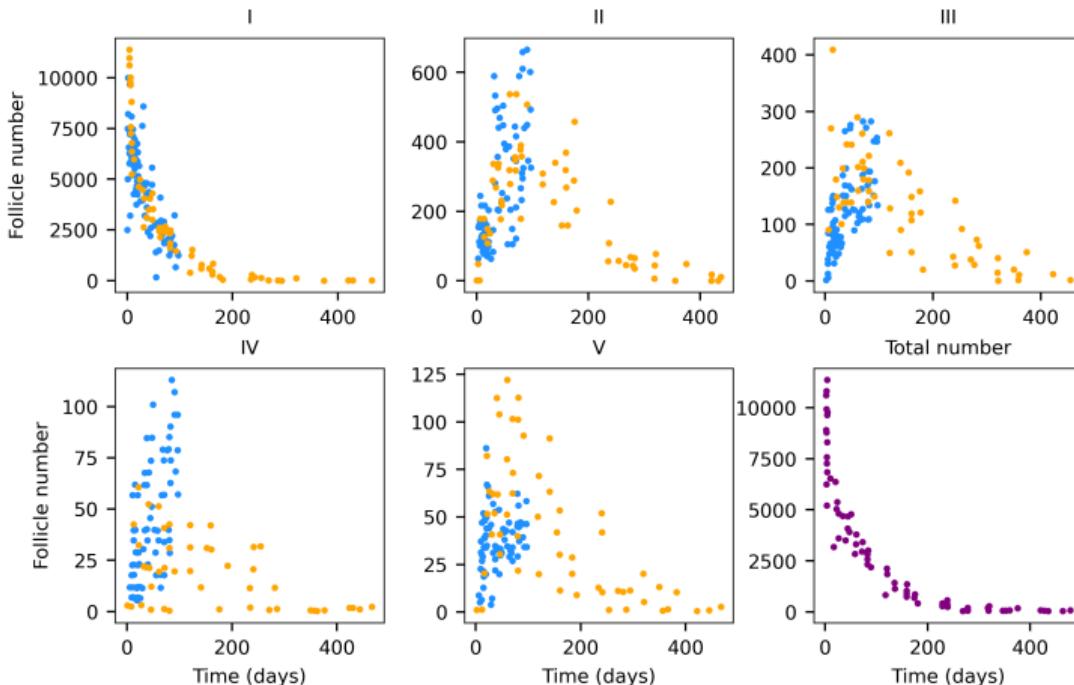
Stochastic compartmental population dynamics

Multiple timescales and order of magnitudes \Rightarrow Model reduction



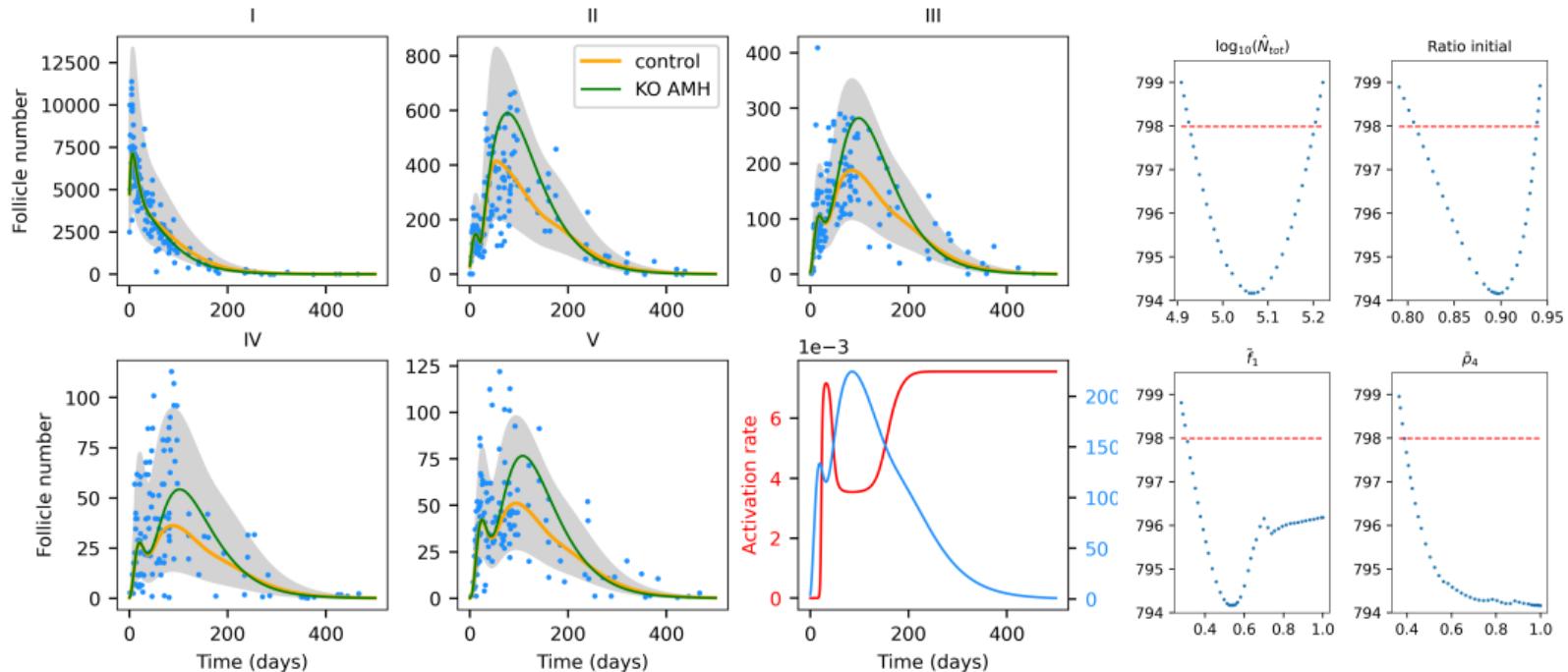
	Transition	Rate
Birth (reserve)	$(X^\varepsilon, Y^\varepsilon) \rightarrow (X^\varepsilon + \varepsilon, Y^\varepsilon)$	$\frac{r_0(Y^\varepsilon)}{\varepsilon} X^\varepsilon$
Maturation (reserve)	$(X^\varepsilon, Y^\varepsilon) \rightarrow (X^\varepsilon - \varepsilon, Y^\varepsilon + e_1)$	$\frac{\lambda_0(Y^\varepsilon)}{\varepsilon} X^\varepsilon$
Death (reserve)	$(X^\varepsilon, Y^\varepsilon) \rightarrow (X^\varepsilon - \varepsilon, Y^\varepsilon)$	$\frac{\mu_0(Y^\varepsilon)}{\varepsilon} X^\varepsilon$
Maturation, $i \in [1, d-1]$	$(X^\varepsilon, Y^\varepsilon) \rightarrow (X^\varepsilon, Y^\varepsilon - e_i + e_{i+1})$	$\frac{\lambda_i(Y^\varepsilon)}{\varepsilon} Y_i^\varepsilon$
Death, $i \in [1, d]$	$(X^\varepsilon, Y^\varepsilon) \rightarrow (X^\varepsilon, Y^\varepsilon - e_i)$	$\frac{\mu_i(Y^\varepsilon)}{\varepsilon} Y_i^\varepsilon$

Data-driven parameter estimation : low-throughput data



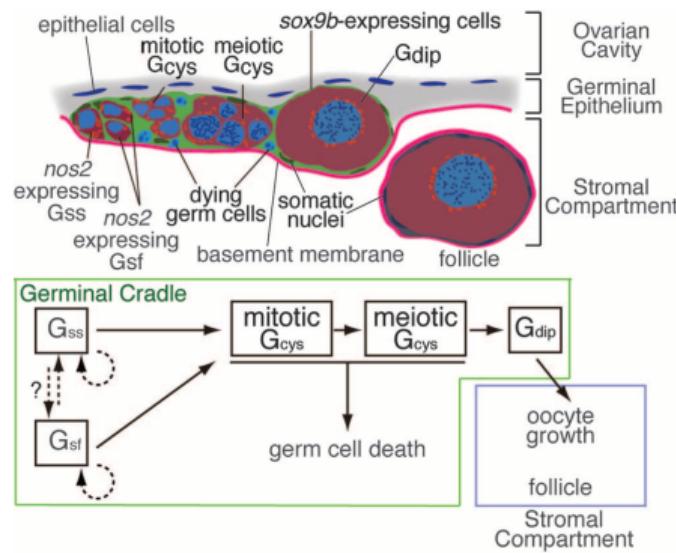
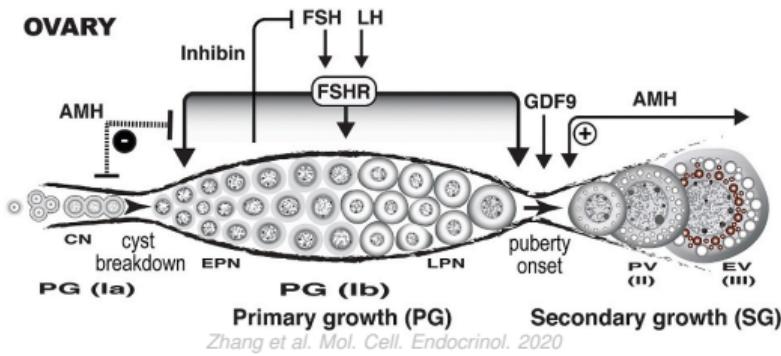
Data-driven parameter estimation : low-throughput data

Model selection, parameter identifiability, perturbation prediction



Knowledge driven modeling approaches (Fish)

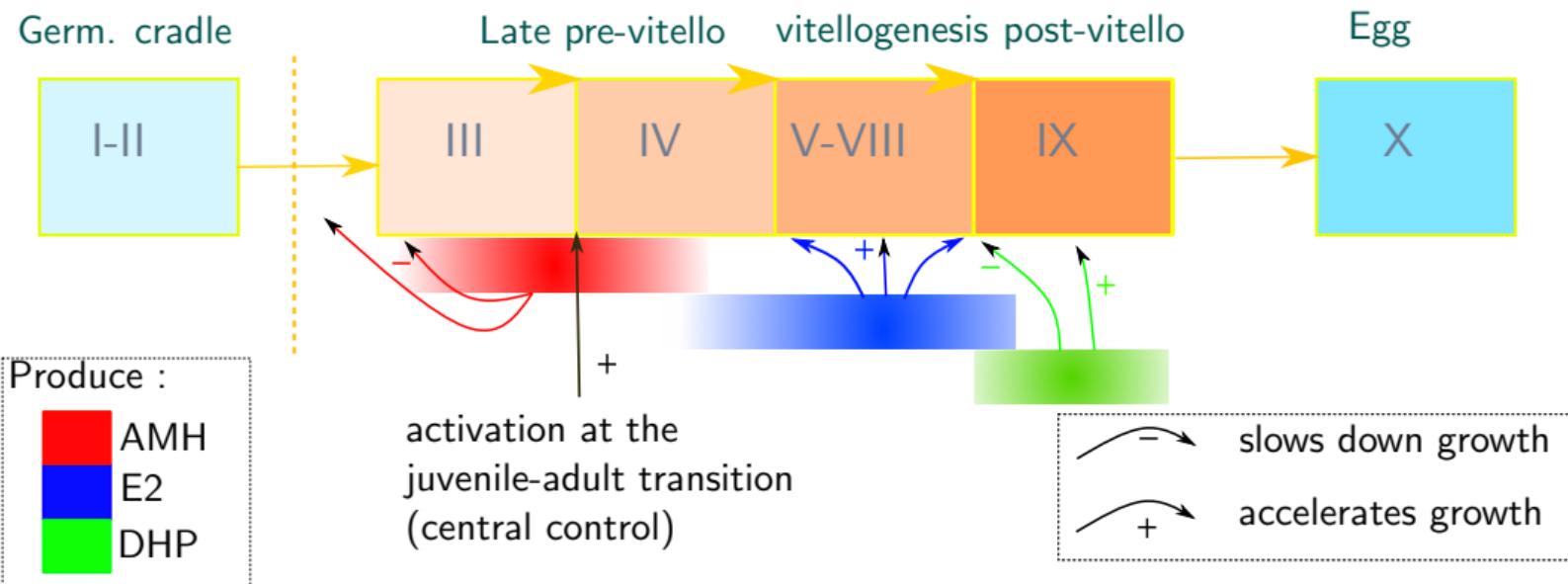
Embedding cell biology/developmental biology/endocrine information



Nakamura et al. Science 2010

Knowledge driven modeling approaches (Fish)

Embedding cell biology/developmental biology/endocrine information



Deterministic size-structured population dynamics

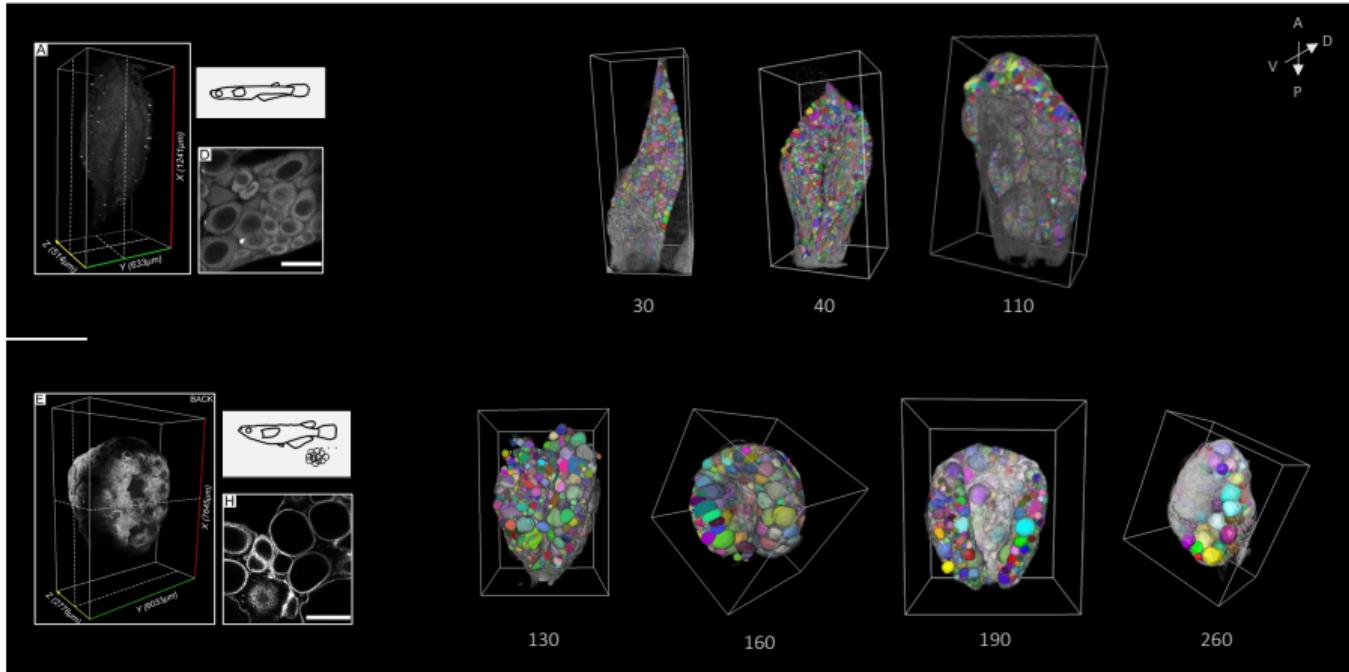
Nonlinear conservation laws: numerical scheme and asymptotic behavior

Parameters	Interpretation	Output	Interpretation
λ_0	Cradle exit rate	ρ_0	number of cells in the cradle
r_0	Cradle renewal rate	ρ	size density from stage III to IX
λ	growth speed from stage III to IX	ρ_1	number of stage X oocytes
W_i	"quantity" of hormone i secreted		

$$\left\{ \begin{array}{l} \frac{d}{dt}\rho_0(t) = r_0(\rho_0)\rho_0(t) - \lambda_0(W_{AMH}(t))\rho_0(t), \quad t > 0 \\ \lim_{x \rightarrow 0} (\lambda\rho) = \lambda_0\rho_0(t), \quad \text{sur } [0, +\infty) \\ \partial_t\rho + \partial_x (\lambda(x, W_{AMH}, W_{E2}, W_{DHP})\rho) = 0, \quad x \in [0, 1], \quad t > 0 \\ \frac{d}{dt}\rho_1(t) = \lim_{x \rightarrow 1} (\lambda\rho) - \text{spawn}(t), \quad t > 0 \\ W_i(t) = \int_0^1 \omega_i(x)\rho(t, x)dx, \quad i \in \{AMH, E2, DHP\} \end{array} \right.$$

Data-driven parameter estimation : DL-based data extraction

Work of Violette Thermes and collaborators

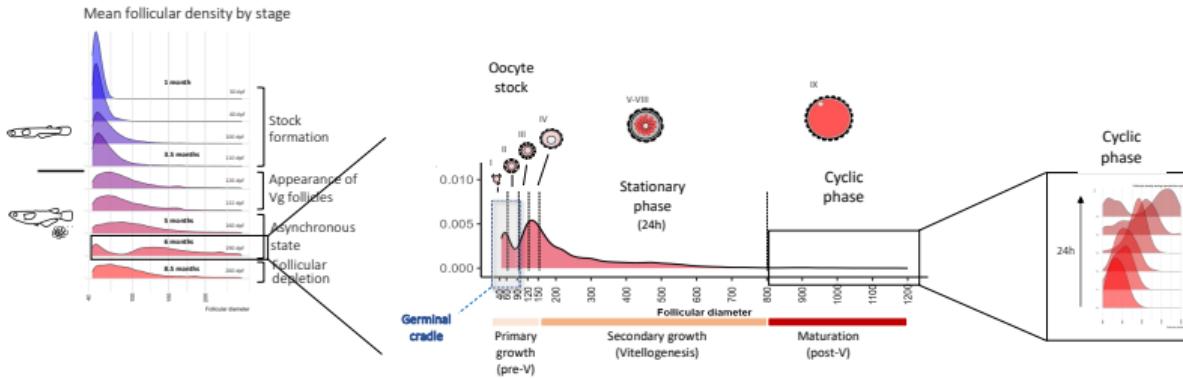
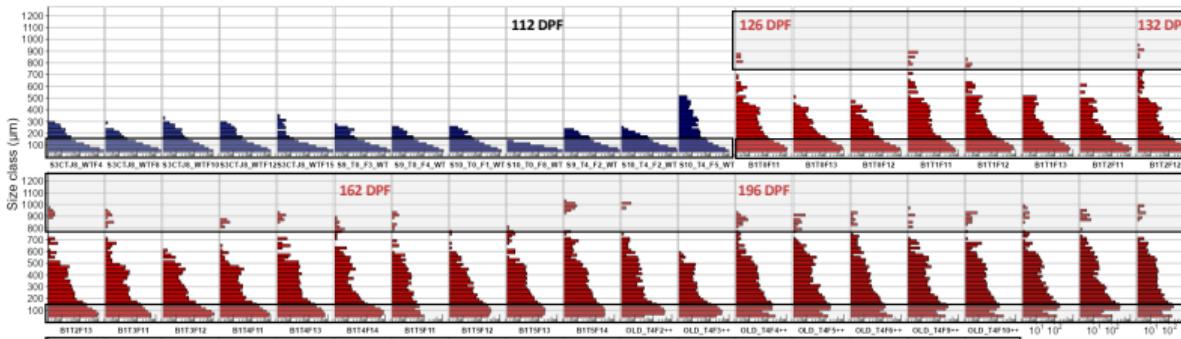


Inputs : 3D ovarian imaging / Automatic follicle segmentation and classification

Outputs : age/space-varying distribution in size/class of the total population of ovarian follicles

Data-driven parameter estimation : DL-based data extraction

Work of Violette Thermes and collaborators

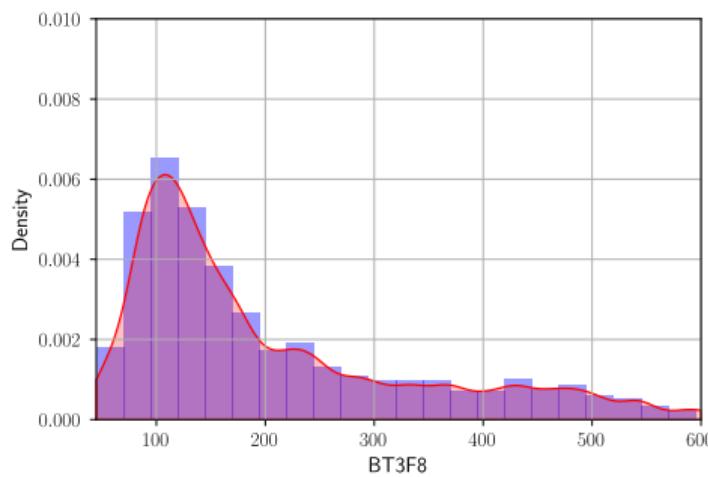
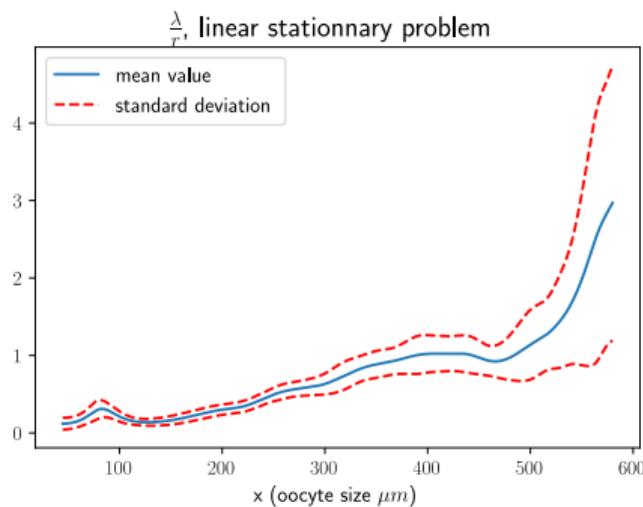


Data-driven parameter estimation

Nonparametric inverse problem on stationary state

$$\begin{cases} \bar{\rho}(0) = r \\ \partial_x (\lambda(x)\bar{\rho}) = 0, \quad x \in [0, 1] \end{cases}$$

Hormonal interactions cannot be deduced from purely stationary data, yet we can infer the size-dependent oocyte growth speed.



Ongoing/ future directions

Stochastic and deterministic models of structured populations with nonlinear and nonlocal terms

- Wellposedness / stationary solutions
- Inverse problems
- Structuring variable(s)
*Coupling with cell dynamics models on the single-follicle level
Spatial distribution*
- Physics-based modeling (morphogenesis)

