# Numerical simulation of the selection process of ovarian follicles : From biology to algorithms

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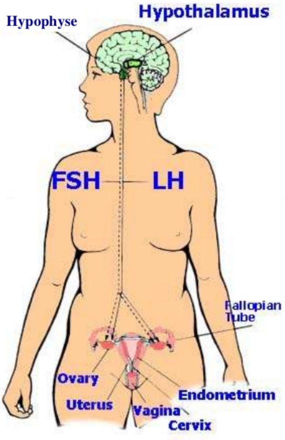
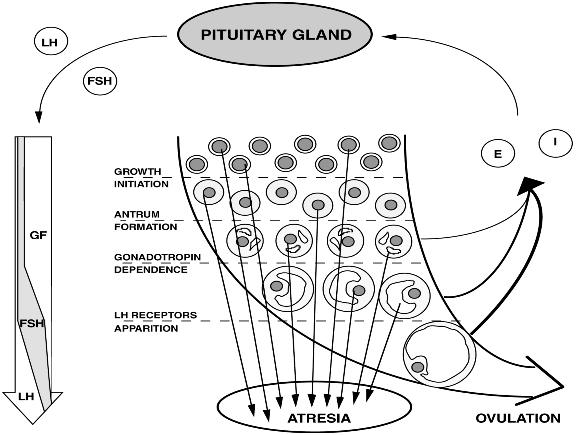
# Introduction : Biological background




*Macro scale : Pituitary gland, ovary.*

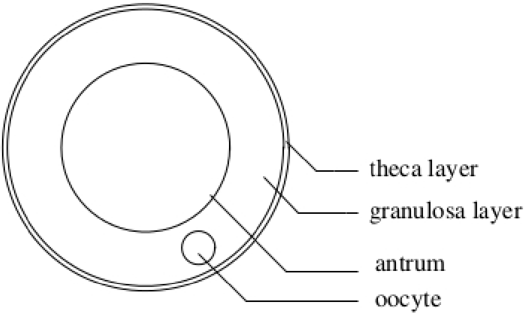



*Micro scale : Chronology of the follicular development.*

# Outline

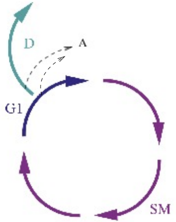
- Multiscale Biological Model
  - Selection process
  - Micro : cell kinetics
  - Macro : closed loop control
- Algorithms
  - Macro : Parallelization strategy
  - Micro : Finite volume scheme
- Numerical simulations
  - Movie
  - Macro variables
  - Parallelization performances
  - Interfaces performances

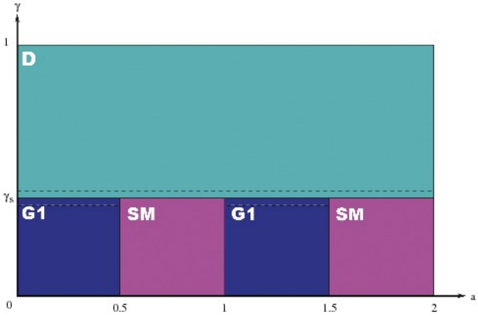
# Model : Follicle




*Scheme of a follicle.*

# Model : Population dynamics




*Granulosa Cell phases.*

# Model : Unknown of the problem

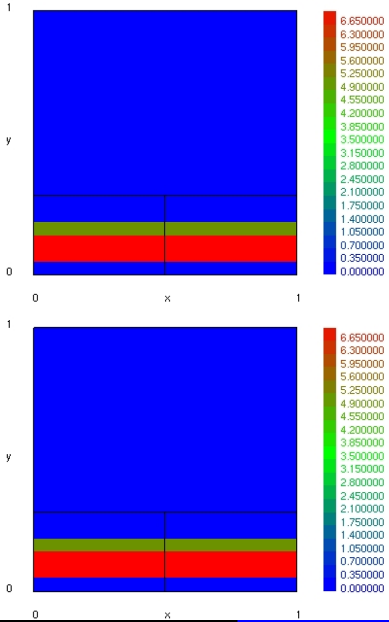
Cell densities of the follicles

$$\begin{cases} \phi_1(a,\gamma,t) \\ \dots \\ \phi_{N_f}(a,\gamma,t) \end{cases}$$

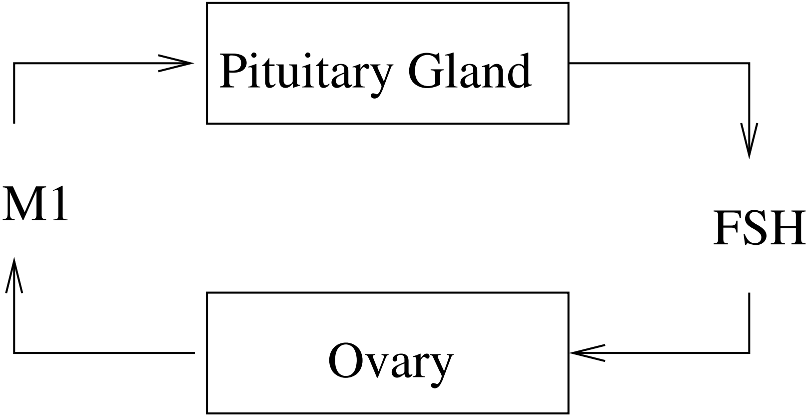
with

$$\begin{cases} a \quad \text{age} \\ \gamma \quad \text{maturity} \\ t \quad \text{time} \\ N_f \quad \text{number of follicles} \end{cases}$$

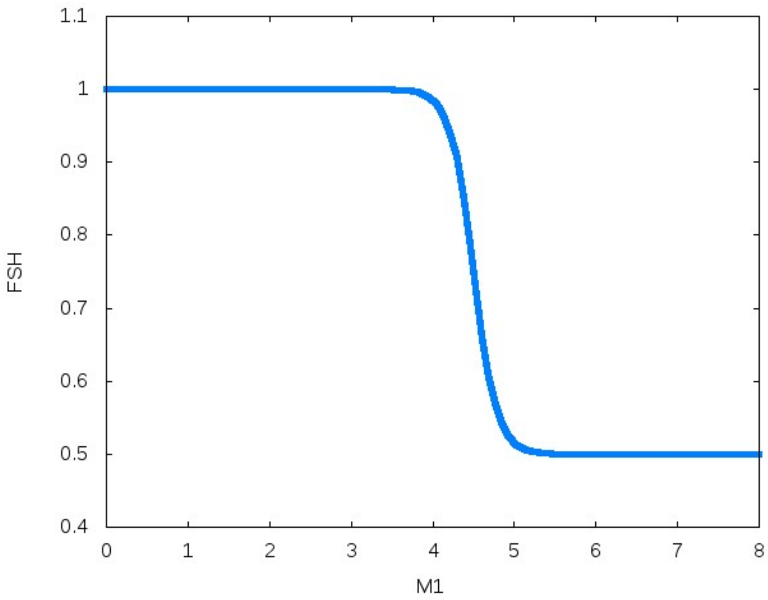
# Model : Example of a set of two follicles



# Model : Closed loop control



# Model : Closed loop control



# Model : Hyperbolic system of conservation laws

Dynamic

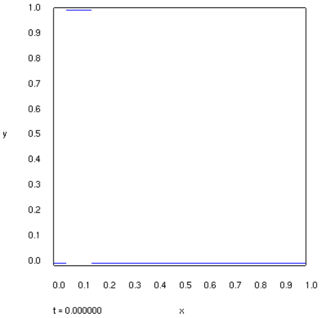
$$\begin{cases} \partial_t \phi_1 + \partial_a g(a,\gamma,u_1(t))\phi_1 + \partial_\gamma h(a,\gamma,u_1(t))\phi_1 = -\Lambda(a,\gamma,U(t))\phi_1 \\ \dots \\ \partial_t \phi_{N_f} + \partial_a g(a,\gamma,u_{N_f}(t))\phi_{N_f} + \partial_\gamma h(a,\gamma,u_{N_f}(t))\phi_{N_f} = -\Lambda(a,\gamma,U(t))\phi_{N_f} \end{cases}$$

Initialization

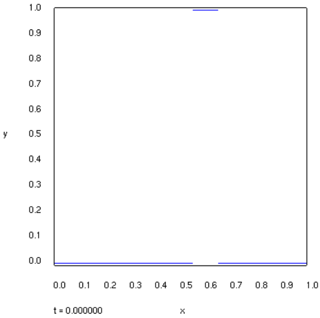
$$\begin{cases} \phi_1(a,\gamma,0) = \phi_1^0(a,\gamma) \\ \dots \\ \phi_{N_f}(a,\gamma,0) = \phi_{N_f}^0(a,\gamma) \end{cases}$$

Periodic boundary conditions.

# Quick reminder on transport equations




a) $t = 0$




b) $t = 0.5$

$$\partial_t \phi + \partial_x \phi = 0$$

# Model : Moments

- Zero order moment (local masses)

$$\begin{cases} m_0(1,t) = \iint_\Omega \phi_1 \mathrm{d}a\mathrm{d}\gamma \\ \dots \\ m_0(N_f,t) = \iint_\Omega \phi_{N_f} \mathrm{d}a\mathrm{d}\gamma \end{cases}$$

- First order moment (local maturities)

$$\begin{cases} m_1(1,t) = \iint_\Omega \gamma\phi_1 \mathrm{d}a\mathrm{d}\gamma \\ \dots \\ m_1(N_f,t) = \iint_\Omega \gamma\phi_{N_f} \mathrm{d}a\mathrm{d}\gamma \end{cases}$$

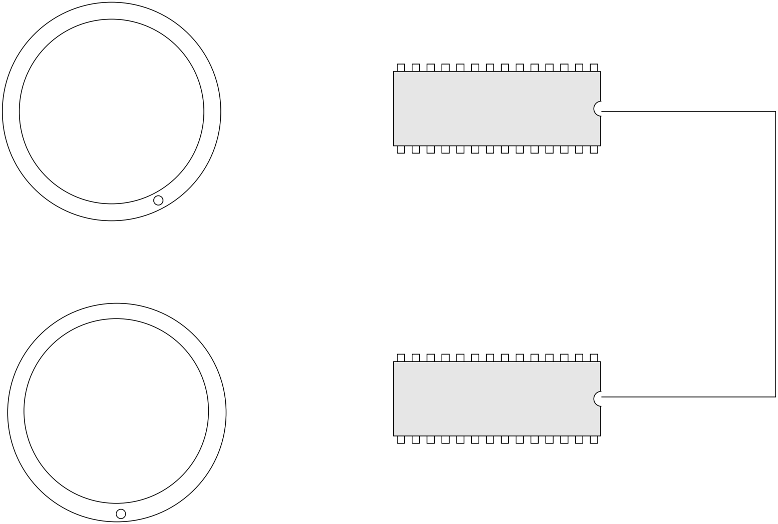
- Sum of the first order moments (global maturity)

$$M_1(t) = \sum_{f=1}^{N_f} m_1(f,t)$$

# Model : Control

- Global control $U = S(M_1)$ (global FSH level)
- Local control $u_f = b(m_f)U$ (local FSH level)
- Particularity of the model : transport equation with controlled speeds

$$\partial_t \phi + \partial_a g(u)\phi + \partial_\gamma h(u)\phi = -\Lambda(U)\phi$$



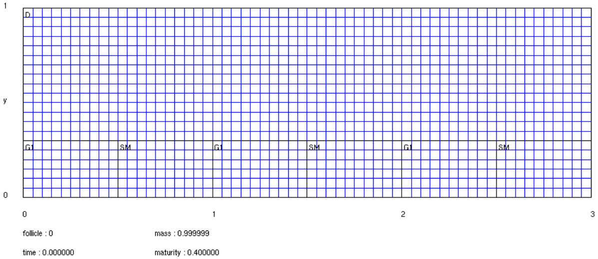
*Analogy with biology.*

# Numerical method : discretization

- Age step $\Delta a$ and maturity step $\Delta\gamma$.
- Time steps $\Delta t^{(n)}$ such that $t^n = \Delta t^{(1)} + ... + \Delta t^{(n)}$
- Mean value approximation in each grid cell

$$\phi_{k,l}^n \approx \frac{1}{\Delta a \Delta\gamma} \iint \phi(a, \gamma, t^n) da d\gamma$$

# Numerical method : computation grid



# Numerical method : finite volume scheme (Micro)

- Finite volume scheme (we note $\Delta x = \Delta a = \Delta \gamma$)

$$\begin{cases} \phi_{k,l}^{n+1} = \phi_{k,l}^{n} - \frac{\Delta t^{(n)}}{\Delta x} D_{k,l}^{n} \\ D_{k,l}^{n} \quad numerical divergence \end{cases}$$

- Stability condition

$$\Delta t^{(n)} \leq \frac{\Delta x}{2max(|g|, |h|)}$$

# Parallelization : communications

High granularity : Few communications at each time step.

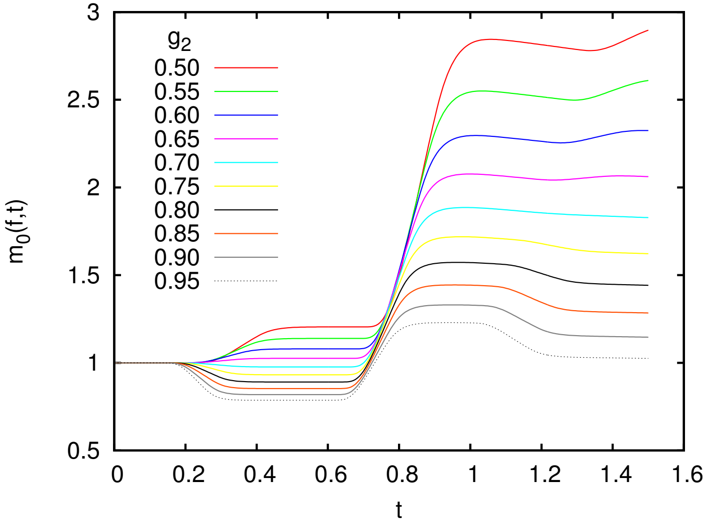
- Computation of global maturity : reduction operation (sum).

$$M^n = \sum_{i=1}^{N_f} m_i^n$$

- Synchronization of the time steps : reduction operation (min).

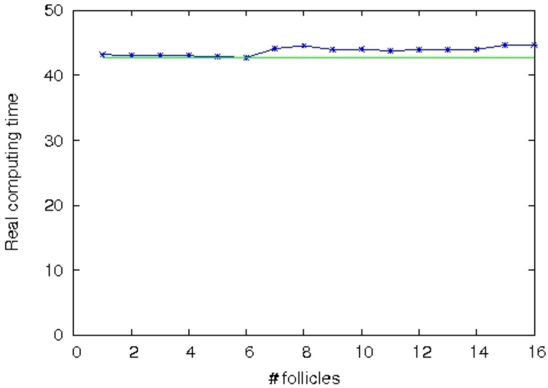
$$\Delta t^{(n)} = min\{\Delta t_1^{(n)}, ..., \Delta t_{N_f}^{(n)}\}$$

# Numerical simulations : Movie




*Macro : Masses during the selection process.*

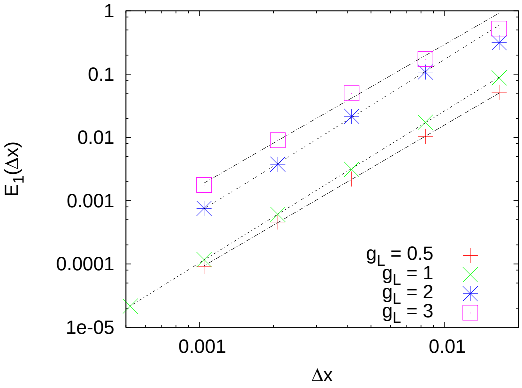
# Numerical simulations : Parallelization performances




*CPU time with respect to the number of follicles.*

Aymard, Clément, Coquel, Postel, Cemracs Proceedings, 2011.
Numerical simulation of the selection process of ovarian follicles.

# Numerical simulations : Interfaces performances




*Test case : Density crossing a doubling interface. Comparison with exact solution (without control). The convergence rate is* 2.4.


Aymard, Clément, Coquel, Postel, Submitted, 2012.
Numerics in cell dynamics : kinetic equations with discontinuous coefficients

Thank you for your attention.