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.
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
Scheme of a follicle.
Granulosa Cell phases.
Cell densities of the follicles

\[
\begin{align*}
\phi_1(a, \gamma, t) \\
\vdots \\
\phi_{N_f}(a, \gamma, t)
\end{align*}
\]

with

\[
\begin{align*}
\{ & a \quad \text{age} \\
\{ & \gamma \quad \text{maturity} \\
\{ & t \quad \text{time} \\
\{ & N_f \quad \text{number of follicles}
\end{align*}
\]
Model: Example of a set of two follicles

Selection process of ovarian follicles
Model: Closed loop control

Pituitary Gland

Ovary

FSH

M1

Selection process of ovarian follicles
Model: Closed loop control

![Graph of FSH vs M1](image_url)
Model: Hyperbolic system of conservation laws

Dynamic

\[
\begin{align*}
\partial_t \phi_1 + \partial_a g(a, \gamma, u_1(t)) \phi_1 + \partial_\gamma h(a, \gamma, u_1(t)) \phi_1 &= -\Lambda(a, \gamma, U(t)) \phi_1 \\
\ldots
\partial_t \phi_{N_f} + \partial_a g(a, \gamma, u_{N_f}(t)) \phi_{N_f} + \partial_\gamma h(a, \gamma, u_{N_f}(t)) \phi_{N_f} &= -\Lambda(a, \gamma, U(t)) \phi_{N_f}
\end{align*}
\]

Initialization

\[
\begin{align*}
\phi_1(a, \gamma, 0) &= \phi_1^0(a, \gamma) \\
\ldots
\phi_{N_f}(a, \gamma, 0) &= \phi_{N_f}^0(a, \gamma)
\end{align*}
\]

Periodic boundary conditions.
Quick reminder on transport equations

\[ \partial_t \phi + \partial_x \phi = 0 \]

a) \( t = 0 \)

b) \( t = 0.5 \)
Zero order moment (local masses)

\[
\begin{cases}
    m_0(1, t) = \int\int_\Omega \phi_1 da d\gamma \\
    \vdots \\
    m_0(N_f, t) = \int\int_\Omega \phi_{N_f} da d\gamma
\end{cases}
\]

First order moment (local maturities)

\[
\begin{cases}
    m_1(1, t) = \int\int_\Omega \gamma \phi_1 da d\gamma \\
    \vdots \\
    m_1(N_f, t) = \int\int_\Omega \gamma \phi_{N_f} da d\gamma
\end{cases}
\]

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

$$\partial_t \phi + \partial_a g(u) \phi + \partial_\gamma h(u) \phi = -\Lambda(U) \phi$$
Numerical method: general strategy

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

$$
\phi_{k,l}^n \approx \frac{1}{\Delta a \Delta \gamma} \int \int \phi(a, \gamma, t^n) da d\gamma
$$
Numerical method: computation grid
Finite volume scheme (we note $\Delta x = \Delta a = \Delta \gamma$)

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

Stability condition

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

High granularity: Few communications at each time step.

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

\[ M^n = \sum_{i=1}^{N_f} m^n_i \]

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

\[ \Delta t^{(n)} = \min\{\Delta t_1^{(n)}, ..., \Delta t_{N_f}^{(n)}\} \]
Numerical simulations : Movie

Selection process of ovarian follicles
Numerical simulations: Macro variables

Macro: Masses during the selection process.
Numerical simulations: Parallelization performances

A numerical simulation of the selection process of ovarian follicles.

CPU time with respect to the number of follicles.

Numerical simulation of the selection process of ovarian follicles.
Test case: Density crossing a doubling interface. Comparison with exact solution (without control). The convergence rate is 2.4.

Numerics in cell dynamics: kinetic equations with discontinuous coefficients
Thank you for your attention.