



Offre n°2024-08077

## Post-Doctoral Research Visit F/M Post-doctoral position in mathematical and/or computational biology : Coupling structured population dynamics models with physiologically-based pharmacokinetic models to assess reproductive fitness

Le descriptif de l'offre ci-dessous est en Anglais

Type de contrat : CDD

Contrat renouvelable : Oui

Niveau de diplôme exigé : Thèse ou équivalent

Fonction : Post-Doctorant

### A propos du centre ou de la direction fonctionnelle

The Inria Saclay-Île-de-France Research Centre was established in 2008. It has developed as part of the Saclay site in partnership with **Paris-Saclay University** and with the **Institut Polytechnique de Paris**.

The centre has [39 project teams](#), 27 of which operate jointly with Paris-Saclay University and the Institut Polytechnique de Paris; Its activities occupy over 600 people, scientists and research and innovation support staff, including 44 different nationalities.

### Contexte et atouts du poste

The postdoc position is open in the framework of two projects led by MUSCA, the [OVOPAUSE](#) ANR project and the [OVOTOX](#) FC3R project, gathering researchers from different institutions and scientific background (applied mathematics, developmental and reproductive biology, ecotoxicology).

The position is an opportunity to be involved in a strongly interdisciplinary consortium, and to strengthen experience in mathematical and computational biology by working on the coupling of population dynamics models with compartmental pharmacokinetic models. The contract is expected to start in the beginning of year 2025, from January to March.

### Mission confiée

The impact of micropollutants on living organisms is a major concern, whether at the individual or population level. Due to their living environment and their physiology, fish are particularly exposed to these micro-pollutants and in particular to endocrine disruptors (ED). They therefore constitute sentinel species for detecting and understanding the multiscale reprotoxic effects of EDs and their adverse outcomes on the reproductive fitness from the individual up to the population levels.

The field of toxicology, and more generally eco-toxicology, has recently acquired methodological tools, such as qAOP (quantitative Adverse Outcome Pathways), based on dynamic models with quantitative outputs to rigorously assess the effects of EDs from available experimental data and knowledge (Conolly *et al.* 2017). qAOP models can predict ED effects *in silico* and be used both for basic research and regulatory purposes, while limiting the use of laboratory animals.

The postdoc work will be dedicated to enriching a qAOP model developed by the hosting team and collaborators. The first task will consist in coupling a size-structured (PDE-based) mechanistic model of oogenesis (the developmental process leading to the release of a fertilizable female gamete), considering all maturation stages and their control (Bonnet *et al.* 2020, Ballif *et al.* 2024), with a physiologically-based pharmacokinetic (compartmental ODE-based) model representing the hormonal dynamics within the reproductive (hypothalamo-pituitary-gonadal) axis (Pery *et al.* 2014, Ly *et al.* 2023). The coupling will be based on careful mapping of functions involved in the different models, addition of missing variables when needed, and timescale separation when possible to enforce model parcimony. The second task will be to design appropriate numerical schemes to simulate the model in both physiological and toxicological situations (exposure to EDs) and perform an extensive parameter estimation and sensitivity/identifiability analysis. The calibrated coupled models will enable a detailed assessment of reprotoxic effects, in particular long-term effects and rebound/compensation mechanisms affecting the oocyte population and hormonal feedback loops.

If time allows, and according to the interest of the post-doctoral candidate, we will tackle a qualitative analysis of the coupled model to shed light onto the structural influence of parameters on the model behavior and the related impact on the reproductive function.

## References

G. Ballif, F. Clément and R. Yvinec, Nonlinear compartmental modeling to monitor ovarian follicle population dynamics on the whole lifespan, *J. Math. Biol.*, 89:9, 2024.  
C. Bonnet, K. Chahour, F. Clément, M. Postel, R. Yvinec. Multiscale population dynamics in reproductive biology: singular perturbation reduction in deterministic and stochastic models. *ESAIM Proc. Surveys*, 67: 72-99, 2020.  
R.B. Conolly, G.T. Ankley, W.Y. Cheng, M.L. Mayo, D.H. Miller, E.J. Perkins, D.L. Villeneuve, K.H. Watanabe. Quantitative adverse outcome pathways and their application to predictive toxicology. *Environ. Sci. Technol.*, 51(8):4661-4672, 2017.  
T.-K. Ly, J. De Oliveira, E. Chadili, K. Le Menach, H. Budzinski, A. James, N. Hinfray, R. Beaudouin. Imazalil and prochloraz toxicokinetics in fish probed by a physiologically based kinetic (PBK) model, 04 December 2023 (preprint available at [10.21203/rs.3.rs-3580808](https://doi.org/10.21203/rs.3.rs-3580808))  
A. Pery, J. Devillers, C. Brochot, E. Mombelli, O. Palluel, B. Piccini, F. Brion, R. Beaudouin. A Physiologically - Based Toxicokinetic Model for the Zebrafish *Danio rerio*. *Environ. Sci. Technol.*, 55848: 781-790, 2014.

## Principales activités

Read and synthesize literature work  
Complete and couple existing models.  
Identify timescale differences in the dynamics to reduce the complete model  
Develop and implement numerical schemes suited for the coupled model  
Perform parameter estimation, sensibility/identifiability analysis  
Write and disseminate the results to the scientific community

## Compétences

Ph.D in applied Mathematics or computational biology, with expert knowledge in numerical simulation of ODEs and PDEs in standard code language (e.g. such as R, Python, Julia, C).  
Experience with either sensitivity/identifiability analysis or parameter estimation will be greatly appreciated.  
Strong motivation for biological applications and work in an interdisciplinary context.

## Avantages

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (after 6 months of employment) and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage

## Rémunération

Gross Salary : 2.788 euros/month

## Informations générales

- **Thème/Domaine** : Modélisation et commande pour le vivant  
Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Ville** : Palaiseau
- **Centre Inria** : [Centre Inria de Saclay](#)
- **Date de prise de fonction souhaitée** : 2025-01-01
- **Durée de contrat** : 2 ans
- **Date limite pour postuler** : 2024-10-31

## Contacts

- **Équipe Inria** : [MUSCA](#)
- **Recruteur** :  
Clément Frédérique / [Frederique.Clement@inria.fr](mailto:Frederique.Clement@inria.fr)

## A propos d'Inria

Inria est l'institut national de recherche dédié aux sciences et technologies du numérique. Il emploie 2600 personnes. Ses 215 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3900 scientifiques pour relever les défis du numérique, souvent à l'interface d'autres disciplines. L'institut fait appel à de nombreux talents dans plus d'une quarantaine de métiers différents. 900 personnels d'appui à la recherche et à l'innovation contribuent à faire émerger et grandir des projets scientifiques ou entrepreneuriaux qui impactent le monde. Inria travaille avec de

nombreuses entreprises et a accompagné la création de plus de 200 start-up. L'institut s'efforce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l'économie.

**Attention:** Les candidatures doivent être déposées en ligne sur le site Inria. Le traitement des candidatures adressées par d'autres canaux n'est pas garanti.

## Consignes pour postuler

### **Sécurité défense :**

Ce poste est susceptible d'être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L'autorisation d'accès à une zone est délivrée par le chef d'établissement, après avis ministériel favorable, tel que défini dans l'arrêté du 03 juillet 2012, relatif à la PPST. Un avis ministériel défavorable pour un poste affecté dans une ZRR aurait pour conséquence l'annulation du recrutement.

### **Politique de recrutement :**

Dans le cadre de sa politique diversité, tous les postes Inria sont accessibles aux personnes en situation de handicap.