Main activities:

- Collaboration with hospitals and other biomedical institutions in France and Germany.
- Funding by public institutions.
- Co-supervision by two experienced INRIA researchers (Dirk Drasdo & Irene Vignon-Clementel).

The main collaborations are with biological research institutions (the Leibnitz Center IfADo, the German Cancer Center in Heidelberg) and the largest liver transplantation center in France, Hospital Paul Brousse/INSERM in Villejuif.

Background:
For many years, we have been carrying out digital simulations to guide the experimental decisions and designs in systems biology of multi-cell systems in liver (e.g., Hoehme et al., PINAS, 2010; Schlies et al., Hepatology, 2014; Drasdo et al., 1 Hepat 2014; Hammad et al., Arch Toxicol 2014; Ghallab et al. et al., 2016; Aubert et al. et J. Biomech Eng 2017). Our simulations are integrated in tissue simulators (Tissim, IfADo), which are modelled on the level of micro-architecture capillaries where the level of tissue level, blood flow and molecular transport are modelled. The system is based on the computer (ideally C/C++) programming and on the end user software Tissim (Tissue Simulator, about 90 thousands of lines of code, plus several specific branches for branches for blood flow, deformable cells etc; Johann et al., to be submitted) but for each new application need to be adapted.

Recently, we were able to demonstrate on some significant examples that models are capable of correctly predicting certain processes using precursor models of the one described above (Schlies et al., Hepatology 2014; Ghallab et al., J. Hepat 2016). The predictions have been validated within the scope of liver regeneration following damage caused by drugs, such as the paracetamol overdose. The discovery of this process has therapeutic potential, as some experiments on animals by our main collaborator indicated that liver regeneration appears to be enabled in vivo. The recent advances in computational fluid mechanics, such as agent-based modeling and multi-scale simulations, will allow us to further improve our models and to better understand the underlying mechanisms.

Mission confiée

In these collaborations we aim to study the processes pertaining to liver disease progression, liver regeneration following damage caused by drugs and after surgery, and, finally, to improve therapeutic decisions and clinical therapeutic concepts. Our long-term mission is to integrate our research procedures and results into the clinical workflow in order to enable the optimisation, in a prospective way, of a patient’s treatment by testing it on the virtual abstract copy of the patient.

The huge amount of information generated through these collaborations needs to be integrated to now calibrate the models and compute the functional consequences of toxic liver damage, as well as of fibrosis and cirrhosis, and toxic liver damage of chronic liver (as an important example of Acute on Chronic Liver Failure). The following few fundamental challenging steps require immediate action: (1) Transfer from animal models (mouse) that were so far used to calibrate our mathematical multiscale models, to the human (patient) situation. (2) Transfer from animal models (mouse) that were so far used to calibrate our mathematical multiscale models, to the human (patient) situation. (3) Link molecular processes and tissue alterations at the level of liver microarchitecture to observables at the level of non-invasive measurement modalities such as biomarkers transported in the blood, and non-invasive imaging (e.g. Diffusion Weighted MRI, Dynamic Contrast Enhanced MRI, Perfusion CT).

The shortest path from biological modeling to the clinical application (step 3) is via computation of the functional consequences of liver disease, which requires sound background in computational mechanics of flows. The 2nd pillar, modeling of disease progression will take longer to bridge from biology to clinics.

The postdoc precise task would be to integrate signaling pathways in drug damage and liver regeneration models, and to extrapolate the consequences on the whole organ by scale and on clinical measurements can be taken. The input would be equally biological and clinical data. After integration of the model components, different disease cases and acute damage have to be simulated. The postdoc should further address the whole liver and whole body scale, and in this sense include the scale that formerly Chloe Audebert, the former PhD student of Irene Vignon-Clementel and Jean Frederic Gerbeau, has addressed (Audebert et al J Biomech 2017, Audebert et al CAMME 2017, Audebert et al and IEEE Trans Biomed Eng 2018). We have been developing and parameterizing models at this large scale based on animal data, but translation to humans is needed.

Informations générales

- **Thème/Domaine**: Modélisation et commande pour le vivant
- **Biologie et santé, Sciences de la vie et de la terre (BAP A)**
- **Ville**: Paris
- **Centre Inria**: CRI de Paris
- **Date de prise de fonction souhaitée**: 2019-11-01
- **Durée de contrat**: 1 an, 4 mois
- **Date limite pour postuler**: 2019-03-17

Contacts

- **Équipe Inria**: MAMBA
- **Recruteur**: Drasdo Dirk / dirk.drasdo@inria.fr

A propos d’Inria

Inria, l’institut national de recherche dédié aux sciences du numérique, promeut l’excellence scientifique et le transfert pour avoir le plus grand impact. Il emploie 2400 personnes. Ses 200 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3000 scientifiques pour relever les défis des sciences informatiques et mathématiques, souvent à l’interface d’autres disciplines. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 160 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.

L’essentiel pour réussir

- **Background in computational fluid mechanics**
- **Engineering, physics or mathematics degree**
- **Open in communicating with people from other scientific disciplines**
- **Flexible and open to acquisition of new skills and knowledge**
- **Experience in model development at tissue level**
- **Experience in model implementation on the computer (ideally C/C++)**

Consignes pour postuler

Candidate’s file:
- **Letter of motivation highlighting the adequacy of the candidate’s training with the proposed subject.**
- **CV**
- **List of publications.**
- **Thesis reports if the thesis has already been defended.**
- **For candidates who have not yet defended, an attestation from the thesis director with a progress report on the thesis / composition of the jury and the probable date of defense.**
- **Letters of recommendation**

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 technologique 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.
Implementation of flow and transport models in C++ in existing software packages (TiSim, LumpedFlow; by INRIA)

Development and refinement of models at multiple spatial scales (intracellular, cell, tissue, organ, body)

Testing and executing intracellular, flow, transport and multiscale simulations

Analysis of biological data including image data

Communication with biological / clinical partners

Writing of documentation, papers and reports

Compétences

INRIA provides a prime environment for simulation of flows, and all our developments of multiscale models in the last years were at INRIA. In order to account for the difficulties given by integrating simultaneously all experimental information to create quantitative predictive mathematical models of liver function, we would need a flow & biological tissue modeller with experience in biological / medical systems and image analysis as input for the generation of the tissue architecture in which the flow and transport processes are simulated, are processed images of different modalities at different spatial scales.

Technical skills and level required: Computational fluid dynamics, transport, knowledge in C/C++, coding

Languages: English necessary, French welcome

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

Rémunération

- Gross Salary per month: 2 653€ brut/mensuel

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.