



The objectives of FragNet are to (a) train a cohort of ESRs across FBLD methods and (b) develop individual skills in research into either new methods in FBLD or to apply FBLD to interrogate biological systems.

We are looking for highly motivated and talented students with a MSc degree who are interested in an ambitious multidisciplinary project on Fragment-Based Lead Discovery (FBLD).

At this moment we have 15 vacancies



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ESR10: Fragment evolution platform – molecular simulations

Host: University of Barcelona, Spain

Academic supervisor: Prof. Xavier Barril (University of Barcelona)

Industrial supervisor: Dr. Armin Ruf (F. Hoffmann-La Roche)

Synopsis

For efficient hit optimisation, a thorough understanding of fragment-protein binding is necessary. Computer-aided drug design (CADD) approaches are able to generate accurate molecular models that integrate available structural data with biochemical and biophysical screening data. In this project, a computational platform will be established that will help to study the binding kinetics of fragment-protein and ligand-protein binding.

Objectives

1. Development of fast simulation-based methods for fragment screening and evolution.
2. Comparison of unbiased (association) and biased (dissociation) MD simulations for binding mode prediction and virtual fragment screening.
3. Integration of simulation-based methods within the fragment evolution platform.
4. Prospective application of simulation-based methods.
- 5.

Approach

The ESR will initially apply computational methods developed in the group (MDmix, Dynamic Undocking) to existing projects, and then proceed to implement advanced sampling molecular dynamics methods that extend the applicability of our current tools. The specific problems of fragment binding mode identification, virtual fragment screening and fragment evolution will be examined with several alternative approaches that will be systematically compared. Optimized protocols will be developed for specific problems and integrated within a fragment evolution platform that will be developed in parallel. The methods will be evaluated prospectively in collaboration with other ESRs.



Qualifications

Required diploma: MSc Computational Chemistry, Bioinformatics or similar degree and a background in chemistry, physics, pharmaceutical sciences or molecular life sciences.

Required expertise: Experience in molecular simulations of biomolecular systems and a solid knowledge of statistical thermodynamics and biophysical methods. Recommended expertise: structural biology, molecular biology or synthetic chemistry would be an advantage. Experience with NMR, ITC, SPR would be highly valued. An interest in computer-aided drug design and strong interpersonal skills are essential to establish fruitful collaborations within the consortium.

Key publications

1. Alvarez-Garcia *et al.* *J. Med. Chem.* **2014**, 57, 8530–8539.
2. Alvarez-Garcia *et al.* *J. Chem. Theory Comput.* **2014**, 10, 2608–2614.
3. Schmidtke *et al.* *J. Am. Chem. Soc.* **2011**, 133, 18903–18910.
4. Seco *et al.* *J. Med. Chem.* **2009**, 52, 2363–2371.



FragNet offers:

- Generously funded positions (duration 36 months) for 15 Early stage researchers (ESRs)
- High profile research projects in an Innovative European Training Network Program
- Excellent facilities for research and education
- Research training in both academic and industrial settings
- Training in state-of-the-art scientific and transferable skills
- Intensive contacts with international collaborators & secondments in other research laboratories

FragNet is looking for candidates that:

- are highly motivated and talented
- are able to work in a multidisciplinary team
- are keen on intra-European mobility to perform PhD research abroad
- have good communication skills

Selection criteria of the candidate:

- fulfil the eligibility criteria (ESR, international mobility) for Marie Skłodowska-Curie Innovative Training Networks (Horizon 2020)
- have a MSc degree in Life Sciences or obtain a MSc degree by September 2016
- have completed a research internship with relevant expertise
- have obtained high grades during his/her studies
- be fluent in English

Application procedure:

1. Send your application mentioning the **ESR number** in the subject line to hrm@fragnet.eu.
2. **Deadline for applications: 31 January 2016.**
3. Please send all the necessary information as **one pdf file** to hrm@fragnet.eu.
 - Detailed **CV** (include information on your BSc and MSc studies, languages, achievements, expertise)
 - **Motivation letter**, addressed to the FragNet selection committee, explaining your motivation why you apply with us. You have to indicate which FragNet ESR project(s) you are interested in (please motivate your selection and indicate which has your preference).
 - Provide contact details of at least 2 references (names, addresses, emails).
 - **Reference letter** from one of the enlisted references
 - Copies of your key educational certificates
 - **Transcript of Records** (i.e. documents enlisting your performance as BSc and MSc student over time by listing the course units or modules taken, credits gained and the grades awarded). If you have not completed your MSc degree yet include all grades obtained so far.
4. You may apply to more than one ESR position. If you do, submit a separate and dedicated application file for each position.
5. If applicable provide a language certificate Application is OPEN 3. The applications will be assessed by the FragNet selection committee, in which all group leaders are represented. Candidates are in particular evaluated on creativity, originality, intellectual capacity and quality of CV and motivation letter. The selection committee also takes into account interdisciplinary and gender balance.
6. Potential (Skype) interviews will be arranged with the group leaders associated with the ESR projects.
7. The ultimate starting date for the ESR projects is: **1st September 2016**, as the complete Fragnet ESR cohort will participate in the first Fragnet workshop that will be organized in York, UK in September 2016.

For other FragNet related questions please contact: info@fragnet.eu

Eligibility criteria

Eligibility criteria of Marie Curie Initial Training Networks apply. Only applicants who comply to the following conditions will be considered:

Conditions of experience (ESR)

Candidates must be, at the time of recruitment by the host organisation, in the first four years (full-time equivalent) of their research careers and have not yet been awarded a doctoral degree. This is measured from the date when they obtained the MSc degree which would formally entitle them to embark on a doctorate.

Conditions of international mobility

Eligible candidates may be of any nationality but must not, at the time of recruitment have resided or carried out their main activity (work, studies, etc.) in the country of their host organisation for more than 12 months in the 3 last years immediately prior to the reference date.



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