

NRC stories

Åsmund Røhr Kjendseth

CV

1995-2001 Cand. Scient., University of Oslo
2001-2002 Military service
2002-2010 PhD, University of Oslo
2008-2012 Time Temp / Keep-it Technologies
2012-2014 Postdoc, University of Oslo
2014-2015 Postdoc, 6 months, NMBU
2015-> Researcher, NMBU (YTR grant)

2003/4 9 months at University of Lübeck
2014 6 months at SNBL, ESRF, France

NRC history

2011

Mechanisms of cyclic-di-GMP signaling in *Bacillus cereus*

Personal Postdoc

- First grant application
- Okay idea (?)
- 8 papers (including reviews)
- 2 pending patents

• Co-supervised 1 PhD and 4 MSc

Strengths of the project: The background to the project is presented well. A good series of collaborations have been put in place and the purification and characterisation of BC0628 provides excellent preliminary data.

Weaknesses of the project: The main issue with the project relates to a lack of information about some of the experiments, some lack of contingency planning, which raises issues with the feasibility of the project. These are presented in detail in the previous sections of the report. Concerns that the project is over-ambitious.

Selected mark : 4 - Good

A good project with potential for improvement

2013

**Biomass degrading lytic
polysaccharide
monooxygenases**
– Resolving molecular
mechanisms through a
combined computational
and experimental

- 13 papers (including reviews)
- 2 patents
- Co-supervised 2 PhD and 4 M.sc.
- 1 manuscript with PEP/Sørli

The project addresses a very important open question that for sure is addressed also in several larger research environments in academia as well as in industry. This is considered a strength and reflecting the relevance, but of course puts special pressure on timely completion of the dissemination of results. The strategy is sound and nicely multidisciplinary and it is possible that the project can lead to breakthrough insight in LPMO mechanisms. However, this is such a challenging area that it is not ensured from the proposal that novel exiting data including LPMOs with optimized activity will be obtained.

Selected mark : 5 - Very good

A project of national and international interest. Publications in recognised journals may be anticipated. The researchers are well merited in their field.

This is a unique and highly original research proposal that aims at describing the active site and enigmatic mechanism of action of the LPMOs, and at generating detailed knowledge about the mode of oxygen activation. This should lead to engineering of more effective and general enzymes, and form a foundation for the synthesis of novel catalysts. There is a very detailed description of the state of knowledge and well formulated good rationales for the study. Computational chemistry and state of the art spectrometric techniques (e.g. synchrotron light EXAFS spectroscopy) are used in a complementary way, which provide validation/calibration of computational data and mechanistic understanding. There is a detailed plan of work, and the applicant has an extensive national and international support. There is also a good plan for training of the PhD student enlisted in the project, including a medium-term (6 months) stay planned in USA to learn more about computational techniques to predict polysaccharide degradation. The project leader has a very good publication record, is well acquainted with the computational and experimental techniques, has experience of working in international research environment, and has experience in teaching and supervising of master and PhD students. The collaborative group of national and international scientists is outstanding and provides the needed complementarity, which makes a perfect match to the research profile of the earlier career PI. There is a good plan for scientific dissemination, but the interaction with stakeholders and the public is vague.

Selected mark : 7 - Exceptional

The project is innovative and at a high international level. In relation to this stage of the career the project manager has scientific qualifications at a high international level, shows independence as a researcher and great future promise. The project group is highly rated.

Why me??

- Original project with interesting approach
- Managed to convince panel; project matched background
- Relevant panel in 2014 (3/7 computational, 1/7 carbohydrate degradation)
- Relevant and excellent partners
- Several publications with PEP/Sørli

2013 application draft



20 days ..



DRAFT – project description

Preliminary title:

Biomass degrading lytic polysaccharide monooxygenases – Resolving molecular mechanisms through a combined computational and experimental approach

Questions

- How do LPMOs activate molecular oxygen and cleave polysaccharides?
- What are the likely reactive oxygen species (H_2O_2 , $\text{O}_2^{\cdot-}$)?
- Is there a link between the electronic structure of different LPMOs active sites and the substrate?
- How do different parts of the protein contribute to active site reactivity and shielding?
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- Are the LPMOs similar to mononuclear copper enzymes as dopamine beta monooxygenase (DBM) and peptidylglycine α -hydroxylating monooxygenase (PHM)?
- What is the role of the hydrophobic residues close to the copper active site? Can this be modeled by including dispersion effects?
- How do LPMOs bind to substrate?

Information needed

- What are LPMO substrates?
- What LPMO origins are known?
- What are the products? (aldonic acids)
- Is the product similar (indicating identical reaction mechanisms)?
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Applications

- Facilitate design of novel catalysts of polysaccharide degradation.

Goals

Combine computational methods with spectroscopy and biochemical data and:

- Identify possible oxygen activation pathways in chitin and cellulose degrading proteins.
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- Investigate the oxidative polysaccharide bond breaking reaction.

Why go theoretical? Want to use theory to investigate reaction mechanisms of lytic polysaccharide monooxygenase where it is very difficult to trap reaction intermediates.

- Identify structural determinates of oxygen activation

Compare QM/MM and cluster approaches

Computational approach

QM/MM calculations (Gaussian09-Amber, Orca- GROMACS)

Cluster calculations (Gaussian09, Orca)

Properties to be calculated

Optimized geometries

Energies

(Redox potentials, free energy perturbation simulations)

Transition states

Potential energy surfaces

Vibrational analysis?

Spectroscopic properties (EPR parameters)

Effects of including dispersion (Conserved Ala and Phe residues)

Available software:

Molecular mechanics and dynamics (Amber)

Docking (Autodock, Glide)

Quantum mechanics (Gaussian 09, Orca)

NCIplot

Computational resources:

Current – Bioportal UiO

Current – Abel – UiO quota

Applying for Notur quota

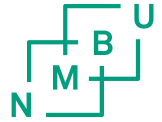
Spectroscopies

EPR spectroscopy (previous – MopE* paper)

Raman spectroscopy (University of Oslo, SNBL, SLS)

X-ray absorption spectroscopy (SNBL/ESRF)

The project description



- Select a topic that is interesting for you and the rest of the world. Start from a perspective and go into details gradually
- What are my expertise? - use it efficiently to make a convincing project. Make the panel believe that you are capable to do the project
- Use your 10 pages efficiently. Do not use one page figures or exaggerate section 3 (section 3&4 half page)
- If you have anyone that can spend time on your proposal – use them. However, many proposals are written in solitude ...

2.4. Budget

Budget information is specified in the grant application form.

3. Key perspectives and compliance with strategic documents

3.1. Compliance with strategic documents

The project conforms to the strategic plan “Kunnskap for Livet (2014-2020)”, NMBU and the National graduate school in structural biology – BioStruct (granted by The Norwegian Research Council), and the National Strategy for Biotechnology 2011-2020: For the future of value creation, health and the environment document.

3.2. Relevance and benefit to society

The project will contribute with increased knowledge about biomass feedstock exploitation and can result in optimized operational biomass degradation processes that are of huge interest to the cellulose based industry and biorefining industries. This is of both great national and global interest.

3.3. Environmental impact

Development of sustainable biofuels will have a great positive environmental impact of the CO₂ balance when replacing petroleum-based fuels. Thus, the project can have potential huge positive effect on the environment by contributing to remove a major bottleneck from modern biorefining processes. There are no negative environmental aspects related to the project.

3.4. Ethical perspectives

No negative ethical perspectives are related to the project. However, the positive ethical aspect of contributing to sustainable use of available biomass to replace consumption of petroleum-based fuels should be considered.

3.5. Gender issues (Recruitment of women, gender balance and gender perspectives)

When employing the PhD student, the female will be selected if two otherwise equal candidates (male and female) apply for the position.

4. Dissemination and communication of results

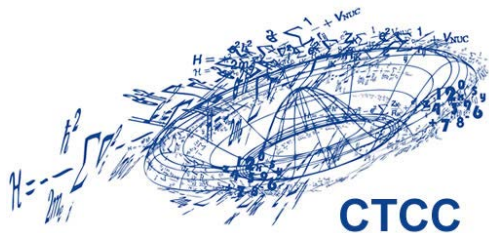
The dissemination plan is stated in the grant application form.

Host, budget and personell

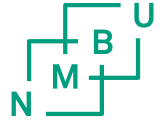
- Select a good host (IKBM is!!)
- If you have several options, consider e.g. overhead
- Ask the department for assistance with the overall budget, this should not take much time
- This year proposals that recruit PhD students and postdocs will be favored

Partners

- Partners should be relevant to the project
- Use your network to find partners; if you contact a person with no introduction prepare to get the silent treatment
- Bring in some solid competence and some rising stars?



Do it! And do it again and again...



- You should start writing this year! Don't wait until you need the grant
- You need the practice, time to massage ideas, and to get some feedback
- And there is always the element of luck ...

For those interested – contact me to see my complete application



"Is it just me or are these review panels getting a lot tougher?"