pNMR Project
Career Development Plan

Name of fellow: Kevin J Sanders - ESR

~~ER~~ ESR

pNMR Project Partner's name : CNRS

Name of Supervisor: Guido Pintacuda

Year 1

Brief overview of research project and major accomplishments expected

The goal of my research project is to develop new methods to study paramagnetic inorganic solids and solid catalysts. Paramagnetic solids suffer from very broad ranges of frequencies, resulting in low intensity peaks that are difficult to uniformly excite via conventional square pulses in NMR. Additionally, paramagnetic samples largely suffer from very short excited lifetimes, so experiments must be sufficiently short enough to manipulate the spins while retaining ample sample excitation. As such, it is my goal to characterize samples through the development of heteronuclear correlation experiments that are both short and broadband. One major improvement in pNMR in "recent" years has been the introduction of SHAPs (Short High-powered Adiabatic Pulses) that are used to adiabatically invert and refocus a broad ensemble of spins; however, adiabatic excitation remains a challenge. One facet of my project will be an attempt to develop an adiabatic excitation scheme, which will eliminate the need for very high-powered conventional excitation pulses. Additionally, following the development of the aMAT experiment by RJ Clément et al (2012), I hope to develop a complementary aPASS experiment. Magic Angle Turning (MAT) has been shown to be erroneous when the lifetime of the sample is very short, but the Phase-Adjusted Spinning Sidebands (PASS) experiment is impervious to short lifetimes. As such, aPASS will be a drastic improvement in the analysis of paramagnetic samples for the correlation of isotropic and anisotropic contributions to the chemical shift.

Secondments planned (amend as necessary) :

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. **Secondment 1**

Start/end date : 01/06/2014 – 31/08/2014
Location (name of the partner, City, Country) : Cambridge, UK

2. **Secondment 2**

Start/end date : 5/01/2015 – 04/04/2015 (subject to change of dates)
Location (name of the partner, City, Country) : Bruker, Germany

3. **Secondment 3**

Start/end date : 01/06/2015 – 31/08/2015 (subject to change of dates)
Location (name of the partner, City, Country) : Cambridge, UK

Long-term career objectives (over 5 years):

1. **Goals:**

To obtain a mastery in broadband adiabatic, heteronuclear correlation experiments to characterize systems containing paramagnetic ions, notably catalysts and energy storage materials.

What further research activity or other training is needed to attain these goals?

My mathematical understanding of the problem is weaker than I would like, and as such I require study of the theory. Additionally, further understanding of the Professors Vaara and Kaupp's description of theory is required to fully understand the paramagnetic effect on a system.

Short-term objectives (1-2 years):

1. **Research results**
   - Anticipated publications:
     1. A publication on the development of aPASS and it's application to paramagnetic solids
     2. Recent and ongoing work on a Ziegler-Natta catalyst has provided interesting results, and I expect this to be published.

   - Anticipated conference, workshop attendance, courses, and /or seminar presentations:
     1. Conferences/Workshops – Mariapfarr, Cambridge, possibly EUROMAR

2. **Research Skills and techniques:**
   - Improvement in the mathematical understanding of the paramagnetic contributions to shift.
   - Improvement in the application of SHAPs to correlation experiments.
   - A better understanding of experimental design and interpretation of data.

3. **Research management:**
   - I hope to improve my ability to work in teams and in proper communication with co-workers.

4. **Communication skills:**
   - I need to improve my scientific writing ability by writing concise and complete thoughts without wasting time. Additionally, I need to expand my scientific vocabulary in order to better communicate my thoughts and arguments.

5. **Other professional training** (course work, teaching activity):
   - Since I live in France now, I must improve my French speaking skills. This will be important at French scientific conferences, not necessarily for me to present my work, but so that I better understand presentations by native French scientists if the presentation is not in English.

6. **Anticipated networking opportunities**
   - I intend to build and maintain a working relationship with Prof. Clare Grey's lab at Cambridge, as I have similar research interests. Additionally I hope to build a better working relationship with my co-workers here at the CRMN.

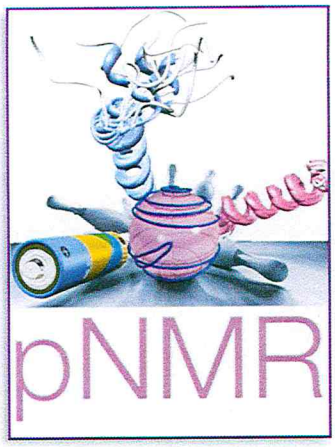
7. **Other activities (community, etc) with professional relevance:**
   - I hope to increase the breadth of my scientific skills, knowledge, and language within NMR to increase my value to future potential employers.

Date & Signature of fellow:

22.1.2014

Date & Signature of supervisor

22.1.14



pNMR Project

Career Development Plan

Name of fellow: Arobendo Mondal

☐ ER ☒ ESR

pNMR Project Partner's name : TUB

Name of Supervisor: Martin Kaupp

Year 1

Brief overview of research project and major accomplishments expected

I am working as a Early Stage Researcher (ESR, PhD student) in the host group at TU-Berlin and focus of the study is to develop the module for the calculations of pNMR shifts for Periodic solids and Surfaces within the CP2K code. This can be divided in several steps

(i) development of the modern pNMR theory
(ii) Formulation of the theory for computational methods
(iii) Implementation of these methods into CP2K code
(iv) Validation of the implementation of the code.
(v) Using the code for possible practical application and experiments
(vi) Explaining and supporting the experimental results by other host groups
(vii) Extending the use and application of the developed code from lab to industry.

During my PhD studies I will cover above mentioned research works which will be followed by modern QC implementation of pNMR shifts for periodic solids and surfaces within the CP2K code, validation of implementation for suitable test cases of solids and surface adsorption sites, application to Li/Fe solids related to battery materials and application to supported catalysts.

Secondments planned :

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. Secondment 1

Start/end date :	March 1st to May 31st , 2014
Location (name of the partner, City, Country) :	ETHZ, Zurich, Switzerland
Group head:	Christophe Copéret
ER involvement :	No
Industrial Associated Partner :	No

2. Secondment 2

Start/end date :	July 1st to September 31st , 2015
Location (name of the partner, City, Country) :	GIOTTO, Florence, Italy
Group head:	Claudio Luchinat
ER involvement :	Yes (Tobias Schubeis)
Industrial Associated Partner :	Yes (CIRMMP)

3. Secondment 3

Start/end date :	October 1st to December 31st ,2015
Location (name of the partner, City, Country) :	(UCAM), Cambridge, United Kingdom
Group head:	Clare Grey
ER involvement :	No
Industrial Associated Partner :	No

Long-term career objectives (over 5 years):

1. **Goals:** Pursue basic Science and continue with academic research as career. NMR and EPR properties study of solid systems (metals, nano-materials, crystal molecules), extending these techniques to study catalytic reactions mechanism and development of materials.

2. **What further research activity or other training is needed to attain these goals?** After my PhD studies, I would like to spend few years as a Post-Doctoral researcher and try to implement ideas which I got during masters studies and will get in my PhD studies. I would like to work on the industrial application and further direct collaborative works with experimental groups for further progress. At this stage the best way to get training is to work on the problems and interactions with experts.

Short-term objectives (1-2 years):

1. Research results

There should definitely be some publications on a successful pNMR implementation into CP2K program. Other than that few could be form implementation of ZFS effects, and then some initial papers on the first applications.

2. Research Skills and techniques:

- Understanding and knowledge of various computational codes regarding to pNMR calculation will be gained.
- Different methods for pNMR calculations, their implementation into codes will be learned.
- Understanding between different theories, approaches and efficiency and ways to improvement in theories will be acquired.

3. Research management:

I will be partly involved in planning, arranging and managing of some of the scientific meetings and conferences. Preparing scientific reports, keeping track of inputs and outputs of the project work. I will also learn working in collaboration with experimentalists and theoreticians at international level.

4. Communication skills:

During my studies I will improve my communication skills both verbal and written to communicate with the scientific community. Optimal communication skills would be acquired for writing scientific papers, making posters, giving talks, presenting posters or being in a conference or meeting

5. Other professional training (course work, teaching activity):

I am attending courses regarding my PhD work and in future I will continue with other courses which will help me in getting a better knowledge of my subject. I will also attend intensive winter and summer school course regarding my studies to get into touch with the experts of the field. I will be also involved in helping other students and newly joined PhD students and project students, which will be helpful for building my teaching ability.

6. Anticipated networking opportunities

Being ITN fellow for pNMR network already connects me to members of the 10 host institutes. Secondments will be helpful to strengthen these bonds with others and would be fruitful for collaborative work. Workshops and conferences will bring us all together at one place to exchange ideas and will be great change to get new openings for collaborations.

7. Other activities (community, etc) with professional relevance:

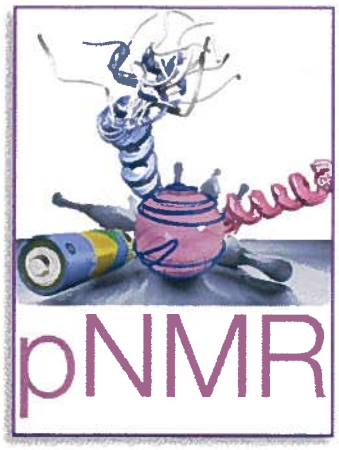
I am looking forward for the opportunities to get interaction with people from the catalysis and material design communities. I believe this program will give me enough opportunities to be linked with the research groups and industries in the field of my interest.

Arobendo Mondal 04/02/2014

Date & Signature of fellow:

04.2.2014

Date & Signature of supervisor



pNMR Project
Career Development Plan

Name of fellow: Syed Awais Rouf

○ ER ◉ ESR

pNMR Project Partner's name : UOULU

Name of Supervisor: Juha Vaara

Year 1

Brief overview of research project and major accomplishments expected

My task as the Early Stage Researcher (ESR, PhD student) in the Oulu node is to focus on the development of the theory and quantum-mechanical electronic structure calculations of NMR chemical shift in paramagnetic systems. The host group has worked on this topic for about 10 years and produced several levels of systematic methods for pNMR shift (nonrelativistic doublet case, relativistically corrected doublet, general theory of higher multiplicities). Due to the fact that paramagnetic metal-containing systems frequently contain low-lying, electronically excited states, there is a need to extend to current methodologies to take systematically into account low-lying excited states, which have a substantial thermal occupation in experimental conditions. Furthermore, the established experimental practice within pNMR is to divide the observed NMR chemical shifts into contact, pseudocontact, and orbital contributions in a way that is not fully compatible with the new advances in pNMR shift theory. Therefore, the two paradigms (experimental and theoretical) need to be brought together, to facilitate further progress in pNMR.

The tasks of my PhD studies will roughly consist of

- Formulation of the modern pNMR theory in a form suitable for experimental spectral analysis
- Extension of the current procedure for calculating pNMR shifts for the strong spin-orbit coupling case
- Extension of the computational methodology from the ground-state manifold to low-lying excited state contributions

In particular, the last two items are strongly coupled to another. The work will start by using Co^2+ -containing complexes and protein models, with three unpaired electrons, as example systems.

Secondments planned:

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. Secondment 1

Start/end date : June 1st-August 31st, 2014
Location (name of the partner, City, Country) : TUB, Berlin, Germany.
Group head: Martin Kaupp. No ER involvement.

2. Secondment 2

Start/end date : between May and August in 2015
Location (name of the partner, City, Country) : BBIO,Rheinstetten, Germany.
Industrial Associated Partner. Group head: Frank Engelke. ER involved: N.N.

3. Secondment 3

Start/end date : between May and August in 2016
Location (name of the partner, City, Country) : BRATISLAVA, Bratislava, Slovakia.
Group head: Vladimir Malkin. No ER involvement.

The periods are indicative, depending on how the project develops in the future.

Long-term career objectives (over 5 years):

1. **Goals:** pursuing academic research, possibly in the field of NMR properties of diamagnetic- and paramagnetic systems (especially materials of interest in medicine and biology).

2. **What further research activity or other training is needed to attain these goals?** After the PhD, I plan to spend one or more years on a PostDoc position.

Short-term objectives (1-2 years):

1. Research results

Critical view on the accuracy of the current theory of pNMR shielding as compared to the experiment on Co^{2+} systems, evaluated for the first time entirely based on ab initio calculations and, hence, not relying on density-functional theory. A manuscript is expected to be submitted for publication during the first half year of the project. Long-range pseudocontact shifts in the same systems are to be evaluated using a point-dipole approximation, providing the first steps towards the project goal of finding a common language for theoreticians and experimentalists. Theoretical investigations of including the low-lying excited-state contributions will have started. Posters and/or talks will presented at project and other meetings.

Research Skills and techniques:A good knowledge of the most important theoretical and computational skills, required for the analysis of pNMR data, will be acquired. The knowledge of usage of many molecular property computing codes will be gained.

2. Research management:

I will be involved in submitting the different scientific reports, and in reaching the different outputs and outcomes of the project.

I will also learn to work with others in a new and international environment.

3. Communication skills:

- Improvement of my language skills, in order to optimally cooperate with scientists inside the scientific community.
- Optimization of all the skills related to the communication of scientific results to the scientific world, like writing scientific papers, posters presentation and taking part to conferences and meetings.

4. Other professional training:

I will be involved in helping and mentoring other students in their work, or starting PhD students (in the future).

I will attend cross cutting training courses organised by my PhD school, such as Scientific English Improvement courses (oral presentations and writing a scientific paper), professional project building, finding a job after a PhD, and how to add value to my research work thanks to social networks.

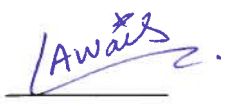
5. Anticipated networking opportunities:

The planned applied trainings and secondments will give me the opportunity to create networks with the involved institutions.
The international workshops organised during the course of the project will give me the possibility to experience scientific networks conference, and to contribute to them.
In parallel, the intensive collaborative network at the host institution will give me the possibility to position my first research experiences within a broad international context.

6. Other activities (community, etc) with professional relevance:

None to report at this time of my PhD.

Date & Signature of fellow:
28/11/2013



Date & Signature of supervisor
28/11/2013

pNMR Project
Career Development Plan

Name of fellow: Roberta Pigliapochi
ESR4
pNMR Project Partner's name : Cambridge University
Name of Supervisor: Clare P. Grey

Year 1

Brief overview of research project and major accomplishments expected

The project aims to develop an overall framework to investigate local structure of paramagnetic materials such as lithium-ion batteries. In a battery the chemical energy is converted into electrical energy through a system made of an anode, in this case the source of lithium ions, an electrolyte, to separate ionic and electronic transport, and a cathode, the sink of the lithium ions and of major interest in this project. The flow of ions and electrons generated from the reaction $Li = Li^{+} + e^{-}$ affects and depends on the structural and electrical properties of the various components of the circuit, making their characterization of central importance. Nuclear Magnetic Resonance (NMR) spectroscopy is a powerful tool for analyzing the related changing of the local structure, and first-principle quantum mechanical studies supplies a theoretical description of the process. Nonetheless, the paramagnetism of the involved systems makes both of the approaches strongly problematic to be interpreted. In particular, the presence of spin-orbit coupling affects g- and hyperfine tensors, which both contribute to the measured shifts and Shift Anisotropy (SA). It is precisely the spin-orbit coupling to be quite demanding to be dealt with computationally, and most of the theoretical approaches don't include it within their formalism. The overall aim of the project would be to formulate a complete DFT method through which this effect could be taken into account in order to reach a better understanding of the NMR experimental data.
The project would base on a recently presented theoretical formalism by Vaara et al. in parallel with a deeper understanding of different computational approaches, functionals and packages. The study would start with model paramagnetic $LiMPO_4$ ($M=Fe^{2+}$, Co^{2+}) cathodes first in order to evaluate the approach, and would then move on to hitherto unstudied or structurally more complicated systems. Referring to a theoretical bond-pathway decomposition of ^{31}P and $^{6/7}Li$ NMR shifts in $LiFePO_4$ and $LiCoPO_4$ phases, the differences found between calculated and experimental $^{6/7}Li$ chemical shifts are thought to be due to the relatively large contribution of the so far neglected spin-orbit effects to the overall Li shift. The treatment of this coupling would be now considered and studied through different approaches (GFT basis sets and all-electron effective core potentials; PW basis sets and pseudopotentials), functionals (hybrid B3LYP, hybrid PBE0, full DFT PBE with the Hubbard +U correction) and packages (CRYSTAL09, CASTEP, CP2K, QuantumESPRESSO). The obtained results would lead to a better insight on how hyperfine and spin-orbit effects are treated quantum-mechanically, and on how influent the presence of transition metals with anisotropic magnetic susceptibility is on the chemical shift of the observed site.
In parallel, improvements to solid-state NMR experiments on the same materials would be carried on through advanced experimental setups in order to obtain data to compare with the computational results.

Secondments planned (amend as necessary) :

The first planned secondment at the TU Berlin would focus on the understanding of spin-orbit coupling and on how it gives rise to g-anisotropy and zero-field splitting. Different theoretical treatments of it would be studied, in order to analyse the quantum mechanical approach and the various implementations. In particular, after having been running hyperfine calculations on $LiFePO_4$, $LiCoPO_4$ and $LiFe_xMg_{(1-x)}PO_4$ with CRYSTAL09 and QuantumESPRESSO codes for the first 6 months in Cambridge, the project would carry on broadening the study of these cases with the CP2K software, for which the Berlin research group offers high expertise.

The last secondment at Bruker Biospin would occur later on during the 3-year project so that more experience regarding possible interesting compounds could have been reached until then and the study of the computational results could have been broadened. Highly advanced experimental approaches would be carried on at Bruker industrial partner, which offers specialised equipments to develop combined fast MAS and low temperature aquisitions.

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. Secondment 1 (M21, 6 months)

1st HALF
Start/end date : 15/06/2014 – 15/09/2014

2nd HALF
Start/end date : 01/06/2016 – 01/09/2016

Location (name of the partner, City, Country) : TUB – Berlin - Germany

2. Secondment 2 (M15, 3 months)

Start/end date : 01/09/2015 – 01/12/2015
Location (name of the partner, City, Country) : BBIO – Karlsruhe – Germany (ER1)

Long-term career objectives (over 5 years):

1. **Goals:**

The overall aim would be to describe a framework to allow structural characterization of paramagnetic compounds: a complete theoretical approach would be presented, which would supply the state of the art solid state pNMR experiments with a detailed analysis of different contributions to the observed chemical shifts.

2. **What further research activity or other training is needed to attain these goals?**
Conferences and trainings on first-principle quantum mechanical calculations of NMR parameters would be useful to achieve a deeper understanding of the computational approaches involved in the project. Detailed analysis of the different softwares would also be of strong help.

Short-term objectives (1-2 years):

1. Research results

- Anticipated publications:

One to two publications to high-impact journals are expected, regarding the development of quantum mechanical models and their implementation.

- Anticipated conference, workshop attendance, courses, and /or seminar presentations:

First year probationary review/CPGS examination at the University of Cambridge (first year written report submission + oral dissertation). Posters and oral presentations at future pNMR training events as well as at various conferences.

2. Research Skills and techniques:

- Training in specific new areas, or technical expertise etc:

Training in different coding languages (Python, C++, Fortran) to be attended during 2014/2015 at the University of Cambridge; learning of various DFT codes (CRYSTAL09, QuantumESPRESSO, CASTEP, CP2K); application of advanced NMR techniques for paramagnetic systems.

3. Research management:

- Fellowship or other funding applications planned

NONE

4. Communication skills:

Communication skills would be practised through group meeting talks. First year probationary review/CPGS examination at the University of Cambridge would be undertaken, which would consist of written report submission and oral dissertation. Posters and oral presentations at pNMR training events and conferences would be given. Manuscripts are expected to be submitted to high-impact journals.

5. **Other professional training** (course work, teaching activity):

Supervision of exercise sessions for master students during the first year; supervision of laboratory experiments for undergraduate and master students throughout all the 3 years.

6. Anticipated networking opportunities

Meetings within the pNMR network and other conferences. Broadening of the experience towards both external Universities (TU – Berlin) and industries (Bruker Biospin).

7. Other activities (community, etc) with professional relevance:

NONE

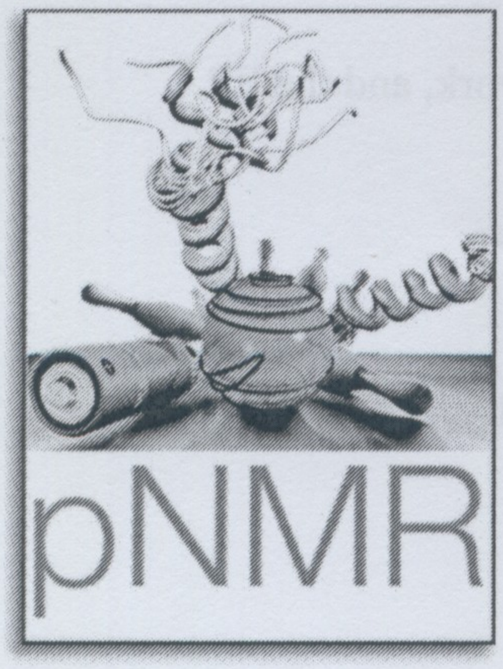
Date & Signature of fellow:

12/05/2014

Roberta Pigliapochi

Date & Signature of supervisor

Clare P. Grey



pNMR Project
Career Development Plan

Name of fellow: Peter Cherry

(•) ER ( ) ESR

pNMR Project Partner's name : Bratislava

Name of Supervisor: Dr. Vladimir Malkin

Year 1

Brief overview of research project and major accomplishments expected

The main aim of the project is to develop and apply new theoretical and computational techniques in the first-principles quantum-chemical software ReSpect. Specific focus will be given to formulation and extension of the relativistic pNMR theory. Computational implementation of new approaches into the ReSpect code, as well as improvement of the existing methodology for fully relativistic calculations of pNMR shifts is expected. Particular attention will be paid to improvement of the efficiency of the current ReSpect code, as this will enable a wider range of systems to be studied. Following successful theoretical development and implementation of these techniques they will be applied to a variety of experimental problems suggested by partners within the pNMR network. Special attention would be paid for rationalization of this development into a form suitable for experimental spectral analysis.

At least three methodological scientific publications are expected to result from this project, as well as results of sufficient quality and quantity to enable and justify active participation in at least one international conference per year. Lectures and presentations of these results at other universities and institutions are also expected.

Secondments planned (amend as necessary) :
Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. Secondment 1

Start/end date : 5/09/2014 until 5/12/2014
Location (name of the partner, City, Country) : Stockholm University, Stockholm, Sweden

2. Secondment 2

Start/end date : 5/09/2015 until 5/12/2015
Location (name of the partner, City, Country) : University of Oulu, Oulo, Finland

3. Secondment 3

Start/end date : 01/04/2016 until 30/06/2016
Location (name of the partner, City, Country): Giotto Biotech, Florence, Italy

Long-term career objectives (over 5 years):

1. **Goals:**
   To develop theoretical approaches to analyze pNMR spectra, i.e.: provide means for improved spectral interpretation for experimental groups and extend the underlying physical theory and quantum-chemical implementations.

2. **What further research activity or other training is needed to attain these goals?**
   Acquisition of a strong grounding in quantum-chemical theory, computer programming and applied computational modelling techniques.

Short-term objectives (1-2 years):

1. **Research results**
   - Anticipated publications: Publications regarding theoretical and methodological development of new techniques for fully relativistic calculation of pNMR parameters.

   - Anticipated conference, workshop attendance, courses, and /or seminar presentations: At least one international conference per year, as well as all relevant training courses and workshops run by members of the pNMR network.

2. **Research Skills and techniques:**

   • Training in specific new areas, or technical expertise etc: Development of new theoretical methods and implementation of these methods in quantum chemical software.

- Verification and further development of such methods through comparison with experimental data and collaboration with experimentalists

3. Research management:

- An active role will be played in the organization and administration of two conferences in Slovakia.
- Identification of areas of further scientific interest and possible research directions.

4. Communication skills:

- Presentations and lectures on conferences and in universities.
- Active participation in workshops.
- Regular collaboration with other institutions in the pNMR network, e.g. University of Oulo, as well as with other institutions outside the network, e.g. University of Tromso, Norway.
- Writing of scientific papers.

5. Other professional training (course work, teaching activity):

- Possible supervision of master students within the group.
- Attend course on effective utilization of supercomputing resources.
- Attending courses on the use of scientific English.

6. Anticipated networking opportunities

- Attendance at conferences and workshops within the field, e.g. 21.2 – 27.2.2014, Mariapfarr, Austria.
- Ongoing collaboration with scientists at the University of Tromso (not part of pNMR network), including research visits of significant duration.

7. Other activities (community, etc) with professional relevance:

- None at present.

Date & Signature of fellow:

18.9.2013

Date & Signature of supervisor

18. September 2013

pNMR

Career Development Plan-Year 1

Name of fellow: Witold Andralojc

Department: CERM

Name of Supervisor: Giacomo Parigi

Date: 09.09.2013

BRIEF OVERVIEW OF RESEARCH PROJECT AND MAJOR ACCOMPLISHMENTS EXPECTED (half page should be sufficient): The principal research project in which I will be involved during the PhD studies, aims at addressing the problem of structural investigation in multidomain proteins with inherent mobility, using the Maximum Occurrence analysis approach developed in CERM. The method allows to partially handle the problem of the reconstruction of the ensemble of conformations sampled by the protein from averaged experimental data by looking for the maximum time a given conformation can exist without violating the experimental data (maximum occurrence) instead of trying to calculate the real probability of existence of that conformation (which is impossible). The next step in the development of this approach will consist of establishing a method of calculating a common value of the maximum occurrence of all conformations forming a relatively small region of the conformation space, which would be much more informative that the values of the maximum occurrence of single conformations. The experimental data for the analysis are NMR parameters related to the presence of a paramagnetic entity in the studied biomolecule (residual dipolar couplings, pseudo-contact shifts and paramagnetic relaxation enhancements). This way the project inscribes itself into a much wider framework of research activity carried out at CERM (often in collaboration with other groups) related to the NMR studies of bio-systems using paramagnetic restraints; the participation in these other projects will also be a major activity during my PhD period. Among them one can mention measuring the temperature dependence of the NMR shifts of the nuclei closet to the iron sulfur center in a high-potential iron-sulfur protein (HIPIP), which should provide valuable information about the electronic structure of this center. A similar project is foreseen for the oxygen evolving complex of photosystem II. Other paramagnetic NMR related projects involving my participation are related one to NMR crystallography (reconstructing the crystal packing of the protein on the basis of known fold and intermolecular paramagnetic NMR restraints) with the protein studied being most probably azurin, and another one to the idea of observing DNP (dynamic nuclear polarization) induced by a paramagnetic metal ion instead of a radical. The above list of projects is not exhaustive and any other research related to paramagnetic NMR conducted in CERM is likely to include my participation.

LONG-TERM CAREER OBJECTIVES (over 5 years):

1. Goals: obtaining the PhD degree and a post-doctoral position and then eventually a permanent position in an academic center.

2. What further research activity or other training is needed to attain these goals?

Following a three years PhD program, involving conducting of research activity and publishing the results obtained. The secondments and conferences provided by the pNMR

network should provide an invaluable source of contacts and links helpful in the query for postdoctoral and then permanent positions.

SHORT-TERM OBJECTIVES (1-2 years):

1. Research results
   - Anticipated publications:
     Yes – depending on the results obtained in the projects described above.

   - Anticipated conference, workshop attendance, courses, and /or seminar presentations:
     Yes – the Marie Curie ITN project pNMR (FP7-PEOPLE-2012-ITN, grant no. 317127) of which the described research is an integral part involves participation in multiple conferences and workshops covering a wide variety of subjects related to paramagnetic NMR. Participation in conferences outside the consortium is also possible depending on the research results obtained.

2. Research Skills and techniques:
   - Training in specific new areas, or technical expertise etc:

   Acquiring experience in performing NMR experiments and analysing NMR data, protein sample preparation for NMR (expression, tagging with paramagnetic ions), the use and development of computational tools for structural determination and the study of conformational heterogeneity.

3. Research management:
   - Fellowship or other funding applications planned (indicate name of award if known; include fellowships with entire funding periods, grants written/applied for/received, professional society presentation awards or travel awards, etc.)

   While receiving the Marie Curie fellowship no search for other funding is foreseen for the moment.

4. Communication skills:

   The participation in the project will help developing skills in writing scientific papers and presenting the results of the conducted research on pNMR conferences (and possibly external ones) as well as gain experience in organizing conferences (in the framework of pNMR) and managing events at the research institution.

5. Other professional training (course work, teaching activity):

   No involvement in teaching in regular courses is foreseen during the PhD program, although after gaining the required experience instructing less experienced coming students to the lab is planned.

6. Anticipated networking opportunities

   As the PhD project is proposed as part of the Marie Curie ITN consortium pNMR (FP7-PEOPLE-2012-ITN, grant no. 317127) it involves multiple networking opportunities by providing secondments (short term stays in other laboratories of the consortium; the closest anticipated secondment is a three months-long leave to Leiden University in order to provide experience in protein tagging) and organizing conferences (with the participation of other groups from the consortium working in protein NMR, but also theoreticians and representatives of the industry).

7. Other activities (community, etc) with professional relevance:

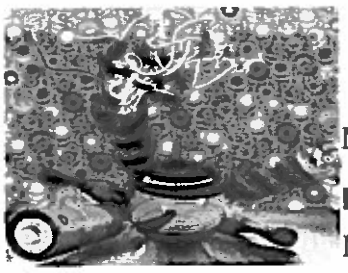
The PhD period will include numerous opportunities to develop soft skills (organization of scientific events, writing research projects etc.) as well as perfecting language capabilities (learning Italian and polishing English in an international environment).

Date & Signature of fellow:

9.09.2013 Witold Andrałojć

Date & Signature of supervisor

9/9/2013



PNMR PROJECT

Career Development Plan

Name of fellow: Shehryar KHAN (ESR 7)

pNMR Project Partners name: Stockholm University

Name of Supervisor: Michael Odelius, Jozef Kowalewski

Year 1

Brief overview of research project and major accomplishment expected.

The prime objective of contrast agents in MRI is to accelerate the relaxation rate of the solvent water protons in the surrounding tissue. Paramagnetic relaxation originates from dipole-dipole interactions between the nuclear spins and the oscillating magnetic field induced by unpaired electrons. Currently gadolinium(III) chelates are the most widely used contrast agents in MRI, and therefore it is incumbent to extend the fundamental theoretical understanding of parameters that drive the relaxation mechanism in order to facilitate their implementation using Quantum Chemical software.

Traditionally the Solomon-Bloembergen-Morgan equations have been utilized to describe relaxation times in terms, primarily of the Zeeman interaction. However, in complexes such as Gadolinium with spins higher than 1 (in this case S=7/2) other interactions such as the Zero Field Splitting begin to play a significant role. This research delves into an understanding of the relaxation process, focusing on the role that zero field splitting and hyperfine interactions play in the relaxation processes associated with clinically relevant complexes. The over all scope of the project is summarized as follows:

-To understand to manipulate, analyze and extract data related to NMR spectroscopy particularly to realize driving mechanisms behind the Zero Field Splitting, by utilizing Quantum Chemical techniques such as Density Functional Theory and wave-function methods(ORCA, DIRAC); and Ab-initio Molecular Dynamics software(CPMD, CP2K)

-To extend results for all-electron relativistic models.

-To compare and contrast existing theoretical & experimental data related to various Gadolinium(III) complexes.

-To make predictions on potentially relevant complexes that have not fully been analyzed/synthesized yet.

-To understand and implement second order perturbations to add to the ZFS Hamiltonian on Gd(III).

-Understanding experimental processes (CIRMMP/Giotto, Italy) : NMRD Profiles and sample preparation.

Secondments planned:

1. Secondment I

Start/End date: Sep/Nov 2014

Location: Slovak Academy of Sciences, Bratislava, Slovakia

1. Secondment II

Start/End date: Jan/March 2016

Location: CIRMMP, Florence, Italy

1. Secondment III

Start/End date: April/ June 2016

Location: Giotto Biotech, Florence, Italy

Long-term career objectives (over 5 years):

1. Goals:

Research in the field of theoretical chemical physics/ theoretical chemistry.

2. What other training needed to attain these goals?

Possibly continuing onto a post doctoral or institutional research position.

Short-term objectives(1-2 years):

1. Research results

Publish at least one scientific paper during the first year. The following plan will be roughly followed:

– **[Oct-Nov]** Benchmarking basis set dependence and scalar relativistic effects on spin-orbit couplings, manifested by Gadolinium(III) on small complexes: e.g Gd^{3+}, GdF_6^{3-}, $Gd(H_2O)_6^{3+}$ in ORCA software to ensure no ZFS at decided level of theory. A comparison of CASSCF/ MRCI and DFT on these systems.

– **[Dec-Jan]** Geometry optimization of basic complexes: $Gd(DOTA)^-$ $Gd(DTPA)^{2-}$ Zero Field Splitting using spin-orbit coupling with DFT and wave function based methods. (ORCA and experiment with Dirac software).

– **[Feb-May]** Use static Ab-initio MD to generate configurations for calculations of ZFS parameters and chemical shifts under periodic boundary conditions for both crystal and solution structures using the CP2K software.

– **[Jun-Aug]** Literature review of experimental and theoretical systems(done in Jan) to assess Gd(III) complex of interest: Create and implement 4 month logical plan using QC/MD methods, focusing on implementing previous techniques to extended systems such as Gd(DO3A).

– **[Sep-Nov]** Internship in Slovakia: Add relativistic effects to system for experimental spectral analysis. Further analysis and assessment (previous system from Feb-Aug)

2. Research Skills and techniques:

-Becoming proficient in theoretical and mathematical models used for determining relaxation parameters.

-Utilizing QM as well as MM techniques for assessing Zero Field splitting parameters.

- Broadening computational skills (familiarity with DIRAC, CP2K, CPMD) as well as becoming completely proficient and comfortable using softwares such as ORCA/NWChem.

3. Research Management:

No other fellowships or funding applications are planned currently.

4. Communication Skills:

Improvement of scientific literature analysis, understanding direct and cursory scientific jargon related to NMR, including terminology used by biologists, physicists and chemists.

5. Other professional training

Build mathematical and computational skills through workshops and courses.

6. Anticipated networking opportunities

A few workshops and conferences are planned for the next year. Also some collaboration with the group in Slovakia (relativistic effects), and a theoretical chemical physics group in Krakow, Poland (not part of pNMR but we plan to collaborate on the initial structure analysis of $Gd(DOTA)^-$ and $Gd(DTPA)^{2-}$ mentioned earlier). In addition these are the other planned workshops I will be attending:

1. A workshop in "Computer Simulations in Chemistry and Physics" at the Chemistry department Stockholm University which collaborates chemistry and physics students with meetings scheduled on a bi-monthly basis.
2. Feb 21st - Feb 25th 2014 at Mariapfarr, Austria, "Electronic and Nuclear Relaxation & Structure Calculations"
3. June 29th - July 3rd 2014 at ETH Zurich, Switzerland, EUROMAR 2014

7. Other activities with professional relevance:

None to report at the moment.

Shehryar Khan

Supervisor: Michael Odelius

pNMR Project
Career Development Plan

Name of fellow:
Mathilde Lescanne

pNMR Project Partner's name :
Giotto Biotech (Florence) /AztraZeneca (Mölndal)/ Zobio (Leiden)

Name of Supervisor:
Prof. Marcellus Ubbink

Year 1

Brief overview of research project and major accomplishments expected

New applications of paramagnetic lanthanide tags.

The research will be aimed at the development of applications of paramagnetic lanthanide tags. In particular, two aspects will be studied. First, the application of the PARAssign assignment method to large, methyl labelled proteins to prove that it is possible to obtain assignments with this approach. Second, the determination of small molecule binding sites and orientations on large proteins, using ligand PCS from several tags attached to the protein. Targets will be selected together with the pNMR Network partner AstraZeneca.

The first year will be dedicated to the production of Hsp90 wild type and of 3 Hsp90 mutants which will be tagged with the probe CLaNP. Ligand binding sites will be characterized with paramagnetic effects. Pseudo-contact shifts on Hsp90 methyl-labelled will be acquired to assign Hsp90 using the software PARassign.

Secondments planned :

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. **Secondment 1**

Start/end date : spring 2014
Location (name of the partner, City, Country) : Giotto Biotech (Florence, Italy)

2. **Secondment 2**

Start/end date : winter 2014
Location (name of the partner, City, Country) : AztraZeneca (Mölndal, Sweden)

Long-term career objectives (over 5 years):

1. **Goals:** post-doc in NMR
2. **What further research activity or other training is needed to attain these goals?**
   - Broaden NMR knowledge and be able to setup new experiments on the spectrometers
   - Lear about paramagnetic effects and use them to assign and study proteins, especially proteins with high molecular mass

Short-term objectives (1-2 years):

1. **Research results**
   - Anticipated publications:

Applications of PARAssign program to real proteins with a high molecular size (>30kDa),
Demonstration of general applicability of protein-ligand structure determination using paramagnetic NMR.

   - Anticipated conference, workshop attendance, courses, and /or seminar presentations:

Reedjik symposium October, 2013 (Annual Institute's symposium)
NWO group meeting in Veldhoven, 9th/10th of December, 2013
Course on protein and protein interactions offered by the University
pNMR courses (see below)
pNMR conferences (see below)

2. **Research Skills and techniques:**

   - Preparation of NMR sample:
   1. Capable of transforming bacteria
   2. Capable of expressing and purifying proteins
   3. Capable of labeling proteins (15N, 13C-methyl)

- Mutagenesis
- CLaNP attachment to the protein
- Setup of NMR sequences on the spectrometer
- Acquisition and processing of NMR spectra (using software as nmrPipe and Topspin)
- Analysis of NMR spectra (using software as ccpNMR, Xplor for docking)
- Programming in Python and extending PARAssign

3. **Research management:**

- none

4. **Communication skills:**

- Attend group meeting twice a month and explain the status of the research to the group
- Present to the group the results of the research and be able to answer the questions about the project
- Make posters to display for conferences and/or scientific meetings
- Be able to speak and write in scientific English
- Attend general courses offered by the University

5. **Other professional training** (course work, teaching activity):

- Supervision of bachelor students (winter 2013)
- Supervision of master student (spring 2014)

6. **Anticipated networking opportunities** (courses and workshops within the Network):
"Liquid and solid-state NMR of paramagnetic proteins" - Florence (IT), September 2015
"Liquid-state NMR of proteins" - Florence (IT)
"NMR in drug discovery" - Leiden (NL)
"Paramagnetic protein tagging" - Leiden (NL)

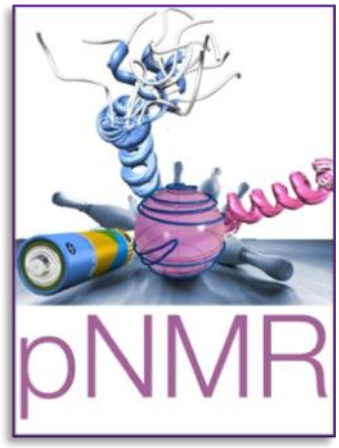
7. **Other activities (community, etc) with professional relevance:**
- Teaching assistant in NMR course at Leiden University

Date & Signature of fellow:

25th of November,

Date & Signature of supervisor

December 16, 2013



pNMR Project

Career Development Plan

Name of fellow: Florian Allouche

(•) ER ( ) ESR

pNMR Project Partner's name : ETH Zürich

Name of Supervisor:Christophe Copéret

Year 1

Brief overview of research project and major accomplishments expected

The Ziegler-Natta process is a key process of the petrochemical industry because it produces a large part of polyethylene. Yet today, the structure of the catalyst active sites is unknown. The development of the catalyst has thus remained empirical and would greatly benefit from a molecular understanding of the active sites. Our long term collaboration has lead to numerous successes in the past with the characterization of surface sites by NMR, the presence of paramagnetic Ti(III) broadens the NMR spectra and leads to unpredictable chemical shifts. In collaboration with Dr. Guido Pintacuda (C- RMN, Lyon), Dr. Vladimir Malkin (Slovak Academy of Sciences, Bratislava) and Prof. Dr. Martin Kaupp (Technische Universitat Berlin), our goal will be to develop molecular approaches to obtain “well-defined” Ziegler-Natta catalyst with a detailed characterization through the development of paramagnetic NMR spectroscopy, the ultimate goal being the rational design of catalysts with predictable surface site signatures.

Secondments planned(amend as necessary) :

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. **Secondment 1**

Start/end date :ca. May during the Ph.D(splitted in 3)
Location (name of the partner, City, Country) : C-RMN Lyon, Lyon, France

2. **Secondment 2**

Start/end date :Splitted in 3 ; currently under discussion
Location (name of the partner, City, Country) : Bruker, Wissembourg, France

3. **Secondment 3**

Start/end date :December 2015 – February 2016 ; the exact timing is under discussion
Location (name of the partner, City, Country) : Slovak Academy of Sciences, Bratislava, Slovakia

Long-term career objectives (over 5 years):

1. **Goals:**After graduating from Ecole Normale Supérieure de Lyon, one of the top schools in France, with a major in inorganic and organometallic chemistry, my goal during my Ph.D is to learn and carry out research, to become autonomous and to develop a critical analytical thinking. My ultime goal is to become to lead a research group in an academic institution.

2. **What further research activity or other training is needed to attain these goals?**

   After completion of my Ph.D and with the goal to enter academia, my plan is to continue in research with a postdoctoral position to explore other fields and to broaden my expertise,.

Short-term objectives (1-2 years):

1. **Research results**

   The main idea is to try to develop model catalysts towards ethylene/propylene polymerization with well-defined active sites, and to use this orthogonal approach to try to further understand the active sites structure of the Ziegler-Natta catalysts widely used in industry. Throughout this project pNMR will be essential to understand the specific signatures of surface (active) sites in view to develop the catalyst via a rational approach.

- Anticipated publications:Publishing in high impact chemistry journalssuch as Angewandte Chemie, JACS ; as well as more journals such as Inorg. Chem., ACS Catalysis, J. Catal…

- Anticipated conference, workshop attendance, courses, and /or seminar presentations: particularly interested into attending workshops about solid-state NMR of paramagnetic materials § inorganic materials and about computational chemistry (electronic and nuclear relaxation, structure calculation, pNMR parameters calculations…)

2. Research Skills and techniques:

- Training in specific new areas, or technical expertise etc:the art of synthesis; Inorganic synthesis of highly reactive compounds under inert atmosphere (Schlenk/Glovebox/High vacuum line techniques); Characterization: NMR of both diamagnetic and paramagnetic compounds (liquid and solid state) UV-Vis, FTIR spectroscopies, XRD, PXRD;Characterization of polymers and computational chemistry.

3. Research management:A monthly individual meeting takes place in order to set up goals and discuss results with Prof. Dr. Christophe Copéret. Furthermore, a group meeting -composed of two literature talks and two research talks - is planned every week so that we are updated about everyone's progress. Finally, there is yearly"review" meeting each year to highlight the came-across problems and establish new strategies towards the research goal.

4. Communication skills:

Presentation skills will be developed through poster presentation, oral communication as well as during the group meeting, where group members need to present his results and novel outcome from the literature (see above research management).
In addition, yearly research reports and manuscript will be written and corrected by the PhD advisor. Currently, a manuscriptderived from the work carried out during the master thesis is currently being written.

5. Other professional training (course work, teaching activity):

With the aim of becoming professor in a close future, I plan to teach laboratory courses as an assistant to strengthen my teaching skills.

6. Anticipated networking opportunities :

Collaboration with Jeschke's group (ETH Zürich) concerning EPR measurements.
Collaboration with Guido Pintacuda (C-RMN in Lyon) and Bruker in Wissembourg concerning NMR and pNMR measurements.
Collaboration with Malkin and Kaup's group concerning theoretical calculations.

7. Other activities (community, etc) with professional relevance:

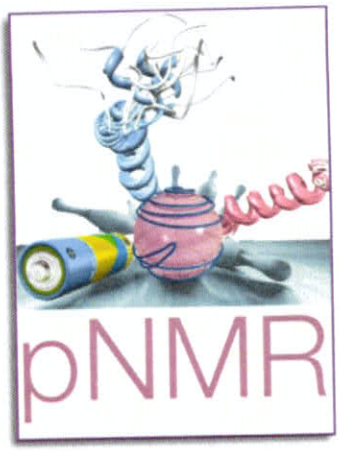
I am responsible for Elemental Analysis and for some analytical materials. I am also training how to perform XRD single-crystals in order to inherit the responsibility as soon as the people already in charge leave.

20.12.2013

Date & Signature of fellow:

20.12.2013.

Date & Signature of supervisor



pNMR Project
Career Development Plan

Name of fellow: Andrea BERTARELLO

○ ER ◉ ESR

pNMR Project Partner's name : CNRS

Name of Supervisor: Guido Pintacuda

Year 1

Brief overview of research project and major accomplishments expected

(half page should be sufficient)

The aim of the project will be the exploration of structure and reactivity of metal centres in metalloproteins as well as in paramagnetically-tagged proteins. In particular, paramagnetic centres in Cu^{II} or Co^{II} enzymes will be investigated, in order to calculate and refine the protein molecular structure, by coupling DFT calculation, MD simulations and NMR hyperfine observable as structure probes. The first candidate protein will be the human superoxide dismutase, loaded with Cu^{II} or Co^{II} ions, for which some preliminary information is already available. This will then allow the exploration of the nature and reactivity of metal species at the core substrate binding and metal ion transport in large membrane-bound metalloenzymes. In parallel to the model system above, proteins containing Fe-S clusters, involved in some fundamental biochemical processes, will also be investigated.

Another aspect of the project will concern paramagnetic protein tagging, a tool for the determination of long-range paramagnetic effects by NMR, which can provide information on the conformation of a protein and on its intermolecular contacts in the solid phase. Protocols for paramagnetic tagging will be developed too.

Secondments are planned with work on both the preparation of paramagnetic tagged samples, and the development of new theoretical methods helping the acquisition and interpretation of paramagnetic effects.

The final goal of the project will be the development of new methods which could combine experimental and theoretical aspects in paramagnetic solid state NMR, in order to answer important questions on the structure and reactivity of proteins.

Secondments planned (amend as necessary) :

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. **Secondment 1**

Start/end date : June/September 2014
Location (name of the partner, City, Country) : Giotto Biotech, Florence, Italy. Industrial Partner. ER involved : Tobias Schubeis

2. **Secondment 2**

Start/end date : September/November 2014
Location (name of the partner, City, Country) : ZoBio, Leiden, The Nederlands. Industrial Associated Partner. No ER involved.

3. **Secondment 3**

Start/end date : July/August 2015
Location (name of the partner, City, Country) : Technical University, Berlin, Germany

The periods are indicative, depending on how the project will be developed in the future.

Long-term career objectives (over 5 years):

1. **Goals:** pursuing academic research, possibly in the field of protein NMR.

2. **What further research activity or other training is needed to attain these goals?**
   After the PhD, I plan to spend one or more years on a PostDoc position.

Short-term objectives (1-2 years):

1. **Research results**

   Scientific papers and conferences attendance, with posters or talk presentations.

2. **Research Skills and techniques:**

   - Acquisition of a deep knowledge of solid state NMR techniques, in particular related to paramagnetic samples in biology. This will include the ability to perform advanced NMR experiments, also in an innovative way, and the use of NMR data in order to achieve useful information for the interpretation of biochemical issues.
   - A good knowledge of the most important theoretical and computational skills, required for the analysis of NMR data, will also be acquired.

- Biochemical skills will be an important aspect too, in particular regarding protein sample preparation and tagging.

3. Research management:

By working within the team leading the pNMR project, I will become familiar with the common administrative and financial management tasks of an EU funded scientific project.
I will be involved in submitting the different scientific reports, and in reaching the different outputs and outcomes of the project.

I will also learn to work with others in a new and international environment.

4. Communication skills:

- Improvement of my language skills, in order to optimally cooperate with scientists inside the scientific community.
- Optimization of all the skills related to the communication of scientific results to the scientific world, like writing scientific papers, posters presentation and taking part to conference and meetings.

5. Other professional training:

I will be involved in elping and mentoring other students in their work, such as M. D. students projects, or starting PhD students (in the future).

I will attend cross cutting training courses organised by my PhD school, such as Scientific English Improvement courses (oral presentations and writing a scientific paper), professional project building, finding a job after a PhD, and how to add value to my research work thanks to social networks.

6. Anticipated networking opportunities:

The planned applied trainings and secondments will give me the opportunity to create networks with the involved institutions.
The international workshops organised during the course of the project will give me the possibility to experience scientific networks conference, and to contribute to them.
In parallel, the intensive collaborative network at the host institution will give me the possibility to position my first research experiences within a broad international context.

7. Other activities (community, etc) with professional relevance:

8. None to report at this time of my PhD.

Date & Signature of fellow:

29/1/2014

Date & Signature of supervisor

29.1.2014

pNMR Project
Career Development Plan

Name of fellow: David A. Bennett

pNMR Project Partner's name : Bruker
Name of Supervisor: Frank Engelke

Year 1

Brief overview of research project and major accomplishments expected
(half page should be sufficient)

The aim of the project is to test and investigate a number of technical advances made at Bruker Biospin. Current topics include:

1. Simpson spectrum simulation
   - general integration in Topspin
   - integration of information typical for pNMR relevant pulse programs
   - integration of optimum control (OC) NMR, cooperation with Nielsen, Vosegaard in Aarhus and/or Tosner in Prag
2. Optimization of LT.MAS hardware and operation for 600WB demo spectrometer for low-temperature measurement of pNMR relevant samples.
3. Focus and sample selection in cooperation with Grey, Cambridge, Pintacuda, Lyon, and Coperet, Zürich
4. Supervision of 3 ESR's. Topics to be determined.
5. Analyzing EFREE technology for dielectrically lossy and/or electrically conducting samples, e.g., battery materials.
6. Implementation of ultrafast MAS probes for paramagnetic samples

Secondments planned (amend as necessary) :
Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. **Secondment 1**

Start/end date : June 2014 – August 2014 (TBC)
Location (name of the partner, City, Country) : Grey, Cambridge, England

2. **Secondment 2**

Start/end date : May 2015 – July 2015
Location (name of the partner, City, Country) : Copéret , Zürich, Switzerland

3. **Secondment 3**

Start/end date : October 2015 – December 2015 (TBC)
Location (name of the partner, City, Country) : Pintacuda, Lyon, France

Long-term career objectives (over 5 years):

1. **Goals:**
   - Possible second Post-doctoral position in the field of NMR
   - Permanent academic or industrial position in the field of NMR

2. **What further research activity or other training is needed to attain these goals?**
   - Networking, e.g. conference and workshop attendance
   - Publishable material in the field of pNMR

Short-term objectives (1-2 years):

1. **Research results**
   - Anticipated publications:
     - Application of NMR to paramagnetic substances
     - Technical documentation (e.g. pulse sequences + software for Topspin)

   - Anticipated conference, workshop attendance, courses, and /or seminar presentations:
     - pNMR Network Wide Training Course MARIAPFARR FEB14 and other pNMR events
     - Chamonix Alpine NMR conference 2015
     - Rocky Mountain Conference 2014

2. **Research Skills and techniques:**
   - Training in specific new areas, or technical expertise etc:
     - General introduction to current pNMR hardware & techniques
     - General introduction to TopSpin
     - Sample preparation for battery materials, catalytic materials and biosolids

3. **Research management:**

   - Fellowship or other funding applications planned
     (indicate name of award if known; include fellowships with entire funding periods, grants written/applied for/received, professional society presentation awards or travel awards, etc.)
     - Not yet available

4. **Communication skills:**
   - Presentation at a Conference relevant to pNMR

5. **Other professional training** (course work, teaching activity):
   - Supervision of PhD students assigned to the project

6. **Anticipated networking opportunities**

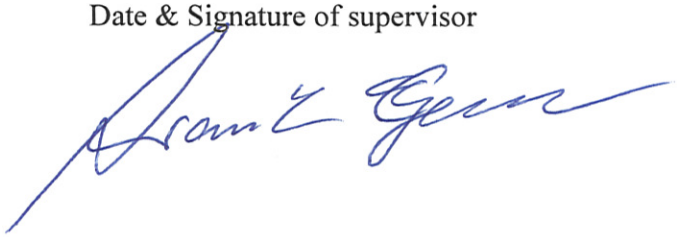
7. **Other activities (community, etc) with professional relevance:**

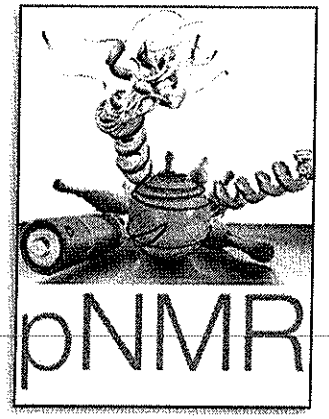
Date & Signature of fellow:

Karlsruhe, 20 Feb. 2014

David Bennett

Date & Signature of supervisor





pNMR Project

Career Development Plan

Name of fellow: Tobias Schubeis

(•) ER ( ) ESR

pNMR Project Partner's name : GIOTTO

Name of Supervisor: Claudio Luchinat

Year 1

Brief overview of research project and major accomplishments expected

(half page should be sufficient)

Recent advances in NMR methodology permit is the measurement of paramagnetic effects in metalloproteins by solution or solid state NMR. Appropriate targets are either proteins that feature incorporated metal ions or proteins that are modified with a paramagnetic tag. My main objectives are the production of isotopically labeled metalloproteins and their preparation for NMR measurements. Among these High potential iron sulfur Proteins (HIPIP), which are well characterized by solution NMR will be investigated in a crystalline form by solid state NMR. This enables the detection of temperature depended changes of paramagnetic chemical shifts, providing information about the electronic structure of the iron-sulfur cluster. Another target is the photosystem II from a thermophile cyanobacterium.

Therefore the cyanobacteria will be cultivated in a fermenter with isotopically labeled CO_2 as the sole carbon source. The photosystem will be purified from the native membrane. The detection of paramagnetic chemical shifts by solid state NMR might provide insight to oxidation states of the oxygen evolving system. Further targets, including paramagnetically tagged proteins, might be added in an advanced stage of the project.

NMR measurement will be carried out at CERM and in collaboration with CNRS, Lyon. The participation in other ongoing projects at CERM is likely.

Secondments planned (amend as necessary) :
Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. **Secondment 1**

Start/end date : tba
Location (name of the partner, City, Country) : CNRS, Lyon, France

2. **Secondment 2**

Start/end date : tba
Location (name of the partner, City, Country) : TU Berlin, Germany

3. **Secondment 3**

Start/end date :
Location (name of the partner, City, Country) :

Long-term career objectives (over 5 years):

1. **Goals:** Sufficient scientific and leadership skills to run a research group in academia

2. **What further research activity or other training is needed to attain these goals?**
   Beside the events of pNMR, networking on international conferences as well as strengthen of my theoretical background of NMR e.g. at the EMBO course.

Short-term objectives (1-2 years):

1. **Research results**
   - Anticipated publications:
     Yes- depending on results

   - Anticipated conference, workshop attendance, courses, and /or seminar presentations:
     Presentation at conferences is depending on the obtained results

2. **Research Skills and techniques:**

   - Training in specific new areas, or technical expertise etc:
     Experience of NMR measurements and data interpretation will be provided at CERM and during pNMR training activities

3. **Research management:**

   - Fellowship or other funding applications planned
     Not planed so far but training in funding and grant application is needed

4. **Communication skills:** Will be improved during the numerous pNMR events

5. **Other professional training** (course work, teaching activity):

6. **Anticipated networking opportunities**
Within the pNMR network and on international conferences

7. **Other activities (community, etc) with professional relevance:**

Date & Signature of fellow:

9.1.14

Date & Signature of supervisor

pNMR Project

Career Development Plan

Name of fellow: Puneet Ahuja

(•) ER ( ) ESR

pNMR Project Partner's name : AZ

Name of Supervisor: Tomas Åkerud

Year 1

Brief overview of research project and major accomplishments expected

(half page should be sufficient)

Paramagnetic NMR offers a powerful means to study protein structures and protein-ligand interactions. Various isotropic and anisotropic effects due to paramagnetic metal ions can be observed at great distances from a paramagnetic centre and can be exploited for structural determination of proteins and protein-ligand complexes. There have been many examples of protein structure determination by paramagnetic NMR but there are few cases of determining structures of protein-ligand complexes. Pseudocontact shifts (PCS) and residual dipolar couplings (RDC) induced by paramagnetic metal ions can be exploited for finding the orientation of small drug molecules with respect to proteins of pharmaceutical interest. Determining the structure of a drug molecule bound to a target protein is highly desired in pharmaceutical industry for enabling more efficient synthetic chemistry efforts in drug discovery. The aim of this research project is to bring the technology of paramagnetic NMR forward to broaden the toolbox of ligand-protein structure elucidation techniques in drug discovery. To achieve the goal, two different strategies of tagging the proteins will be explored: 1) Attaching a Lanthanide tag to a pair of surface cysteine residues inserted by mutations at various positions on the surface of a protein. 2) Inserting lanthanide binding peptides in flexible loops of a protein. The proteins of our interest are HSP90, PTP1B and PGDS which have proven pharmaceutical importance. There are in-house crystal structures of many ligands bound these targets and a considerable amount of information about their binding is available in AstraZeneca to support this project.

Secondments planned (amend as necessary) :

Specify which secondment takes place at an industrial partner of the network, and the ER involved during this particular secondment.

1. **Secondment 1**

Start/end date : From 15th May, 2014 to 22nd July, 2014.
Location (name of the partner, City, Country) : Giotto Biotech S.r.l. , Florence, Italy.

2. **Secondment 2**

Start/end date : From 18th August, 2014 to 3rd October, 2014.
Location (name of the partner, City, Country) : Leiden University , Leiden, Netherlands.

Long-term career objectives (over 5 years):

1. **Goals:** My goal is to establish myself as a successful scientist in structure and biophysics domain of drug development in pharmaceutical industry. This pNMR network training in AstraZeneca which involves collaborations with different academic and industrial pNMR partners, will provide me with many required experimental skills and interpersonal communication skills required to achieve my goals.

2. **What further research activity or other training is needed to attain these goals?**
   As acquiring a broader set of skills is highly recommended in pharmaceutical industry, therefore, acquiring training in other biophysical techniques such as SPR, MS, etc, and wider protein expression skills would be an advantage to attain these goals.

Short-term objectives (1-2 years):

1. **Research results**
   - Anticipated publications:

   Atleast two publications in international peer reviewed journals.

   - Anticipated conference, workshop attendance, courses, and /or seminar presentations:

Meeting:

pNMR meeting, 23rd – 26th September 2014, Cambridge, United Kingdom.

Courses:

1) Solution and Solid-state NMR of Paramagnetic Molecules, 13th – 19th July 2014, Florence, Italy.

2) NMR Relaxation Theory, 19th -20th July 2014, Florence, Italy.

3) Paramagnetic tagging for drug research, 18th - 22nd August 2014, Leiden, Netherlands.

2. Research Skills and techniques:

- Training in specific new areas, or technical expertise etc:

I will gather many new technical expertise and training in many new areas, such as protein construct designing and expression, paramagnetic tagging of various proteins by different methods, computational skills, etc.

I will learn to operate the automated system at AstraZeneca for running NMR experiments of for screening a large number of compounds.

I will get exposure to cutting edge research going on at industrial R&D platform of AstraZeneca which would also provide me with possibilities of both, in-house and external collaboration.

3. Research management:

- Fellowship or other funding applications planned
  (Indicate name of award if known; include fellowships with entire funding periods, grants written/applied for/received, professional society presentation awards or travel awards, etc.)

4. Communication skills:

I will work in collaboration with different groups with extensive expertise in paramagnetic NMR methodology which would give me opportunities to develop different interpersonal skills of team working with different scientists.

As a part of Structure and Biophysics team at AstraZeneca R&D Mölndal, I will develop skills to interact and work with different people incharge of various laboratories and resources.

During my training as an experienced researcher (ER), I will make many presentations about the progress of my project and will make presentations (oral / poster) during various courses and meetings. This would grant me with various communication and presentation skills.

I would like to submit my research work to international journals which would grant me with writing skills for international journals.

5. Other professional training (course work, teaching activity):

6. Anticipated networking opportunities

pNMR network is a collaboration of excellent scientists across academia and industry. During my training as an ER, I will participate in various courses and meetings which would give me with numerous networking opportunities with wide variety of scientists from different research areas.

AstraZeneca is one of the largest pharmaceutical companies with a strong focus on research and development in drug discovery. Here, I attend many seminars and meetings. That gives me many opportunities to interact and collaborate with various scientists from different areas.

7. Other activities (community, etc) with professional relevance:

I am a part of postdoc community of AstraZeneca which is a network of postdocs across all the R&D sites of AstraZeneca. I am active on linkedin where I am connected to many scientists and professionals in other domains.

Date & Signature of fellow:

17/04/2014

Puneet Ahuja

PUNEET AHUJA

Date & Signature of supervisor

17 April 2014

TOMAS ÅKEROD