Natacha GILLET
*Date of birth* March, 2nd 1988
*Professional address* Kaiserstr 12
76131 KARLSRUHE
*Phone number* +49 721 / 608 45704
*E-mail* natacha.gillet@kit.edu

## DIPLOMAS

*2014* PhD in Theoretical Chemistry - Laboratoire de Chimie Physique Université Paris Sud (Orsay, France) et Departamento de Quimica Fisica y Analitica Universitat Jaume I (Castellon, Spain)

*2011* Master degree in Molecular Chemistry – UPMC, ENS (Paris) – *Magna cum laude*
ENS diploma – ENS (Paris)

*2009* Bachelor's degree in Chemistry – ENS (Paris) – *Magna cum laude*

## RESEARCH EXPERIENCE

**Post-Doctoral Positions**

*January 2016-Present* Humboldt Fellowship – Institute of Physical Chemistry Karlsruhe Institute of Technology, (Karlsruhe, Germany)

*June 2015-December 2015* Post-doctoral position – Institute of Physical Chemistry Karlsruhe Institute of Technology, (Karlsruhe, Germany)

**Thesis and Internship**

*August 2014 – September 2014* Internship – Department of Physics Freie Universität (Berlin, Germany): *MM Study of the Release of Thymine Molecule from DNA-Thymine DNA Glycosylase Complex*

*October 2011 – July 2014* Thesis – Laboratoire de Chimie Physique Université Paris Sud (Orsay, France) and Departamento de Quimica Fisica y Analitica Universitat Jaume I (Castellon, Spain): *Numerical Simulations of Intertwined Electrons and Protons Transfers in Proteins*

*February 2011 – July 2011* Master 2 Internship – Laboratoire de Chimie Théorique UPMC (Paris): *Towards Better Understanding of Reaction Pathways using Topological Analysis: from Organic Chemistry to Biochemistry*

*February 2010 – July 2010* Master 1 Internship - Metal·lothioneïnes: relació estructura-funció i aplicacions biotecnològiques Universitat Autónoma de Barcelona (Bellaterra, Spain) : *Study of Pb2+Binding to the Independent αMT3 and βMT3 Domains of the Mammalian MT3Metallothionein Isoform*

*July 2009* L3 Internship - Laboratoire de biochimie des micro-organismes : enzymologie, métabolisme et antibiotique ENSCP (Paris) : *Structural and Mechanistic Study of AnaB, a Flavoprotein Involed in Anatoxin-a Biosynthesis*

*November 2008* L3 Internship– Laboratoire de Chimie Physique Université Paris Sud (Orsay) : *Protonation States Variations of Two Fluorescent Proteins Functions of pH*

**Summer Schools**

*November 2011* RFCT School 2011 – Dourdan (France): *Spectroscopy in Silico*

*July 2010* University of Heraklion (Heraklion, Greece): *from Chemistry to Biology & Medicine via Metals*

## RESEARCH INTERESTS

Proteins and biological systems, protein dynamics and structure-properties relationship, enzymatic process, free energy calculation at classical and QM/MM level, electron transfer in biological media

## REFERENCE SCIENTISTS

Pr. Isabelle Demachy isabelle.demachy@u-psud.fr +33 (0)1 69 15 44 45
Dr. Aurélien de la Lande aurelien.de-la-lande@u-psud.fr +33 (0)1 69 15 73 98
Pr. Vicent Moliner moliner@qfa.uji.es +34 964 728 084
Pr. Marcus Elstner marcus.elstner@kit.edu +49 (0) 721 / 608-45705

## COMPUTER SOFTWARE AND PROGAMMING

deMon2k, gaussian09, Turbomole, CHARMM, NAMD, Gromacs, cuby, fDYNAMO, VMD, blender.
R
Fortran, C, C++, Tcl.

## AWARDS AND TROPHIES

*2013* French l'Oréal-UNESCO *for women in science* fellowship

## OTHER EXPERIENCES

**Teaching**

*January 2016-now* Supervision of a master-PhD student, Institute of Physical Chemistry Karlsruhe Institute of Technology, (Karlsruhe, Germany): charge transfer and protonation mechanisms in cryptochrome and photolyases

*July 2016 – September 2016* Supervision of an internship student (BA) Institute of Physical Chemistry Karlsruhe Institute of Technology, (Karlsruhe, Germany): Computational study of the impacts of mutations on charge transfer in PhrA.

*June 2014 – July 2014* Supervision of an internship student (BA) Laboratoire de Chimie Physique Université Paris Sud (Orsay): *Study of the Deprotonation of L-lactate in the Carbanion Mechanism in Flavocytochrome b2.*

*2011-2013* Université Paris Sud:

- lectures and tutorials in atomistic (L1)
- practicals in solution chemistry (L2)
- tutorials in inorganic chemistry (Master 1)
- Practicals in statistical thermodynamics (Master 1)
- Practicals in computational biochemistry (Master 2)

**Popularization of science**

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|---|---|
| *2014* | Participation in the French l'Oréal program *for Girls in science* |
| *November 2013 – July 2014* | Exhibition (production, website) « *Sur les traces de Pasteur* » la Maison des Sciences Châtenay-Malabry. |
| *May 2012* | Article « *Vache folle et Prions : quand les protéines attaquent le cerveau ! »* on the web site http://culturesciences.chimie.ens.fr |
| *October 2011* | Exhibition (hosting) « *Chimie d'aujourd'hui, monde de demain » (Today chemistry, futur world),* Scientipôle Savoirs et Société |
| *2008-2009* | Science courses at primary schools – la Maison des Sciences Châtenay-Malabry. |

## RESEARCH COMMUNICATIONS

**Oral communication in congress (*: presented by)**

**Understanding Charge transfer in Cryptochromes and Photolyases via QM/MM studies: Application to PhrB protein**
Gillet, Natacha*; Holub, Daniel; Lüdemann Gesa; Elstner Marcus *ISQBP President's Meeting* Bergen, Norway (June 2016).

**QM/MM study of L-lactate oxidation by Flavocytochrome *b2***
Gillet, Natacha*; Ruiz-Pernia, Javier; Demachy, Isabelle; Lévy, Bernard; Lederer Florence; de la Lande, Aurélien; Moliner, Vicent *Theory Workshop 'Computer Simulation and Theory of Macromolecules'*, Huenfeld Monastery, Germany (May 2016)

**Computational Chemistry Tools for Biological Electron Transfers**
Gillet, Natacha*; Elstner, Marcus *Network Meeting of the Alexander von Humboldt Foundation*¸ Düsseldorf Germany (March 2016)

**Description d'un transfert d'hydrure en transferts d'électron et d'hydrogène dans la protéine EmoB**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; de la Lande, Aurélien *RCTF 2014,* Paris France (July 2014)

**Electron and Hydrogen Atom Transfers in the Hydride Carrier Protein EmoB**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; de la Lande, Aurélien *iCHAT 2014,* Monteporzio Catone Italy (June 2014)

**Mechanism of hydride transfer between flavins.**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; Piquemal, Jean-Philip; de la Lande, Aurélien *Theobio 2013*, Götheborg Sweden (June 2013)

**Seminar**

**Effects of protein environment on charge transfers: QM/MM studies**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; de la Lande, Aurélien *Department of Chemistry* University of Basel (October 2014)

**Hydride transfer in EmoB and Fcb2 Proteins: Two different QMMM studies**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lederer, Florence; Lévy, Bernard; Ruiz Pernia, Javier; de la Lande, Aurélien *Department of Physics* Freie Universität Berlin (January 2014)

**Poster**

**Different QM/MM Approaches for Electron Transfers in Proteins**
Gillet, Natacha*; Elstner, Marcus *Theory Workshop 'Computer Simulation and Theory of Macromolecules'*, Huenfeld Monastery, Germany (March 2017)

**Electronic Coupling Calculations for Bridge-Mediated Charge Transfer in Organic and Biological Molecules**
Gillet, Natacha*; Berstis, Laura; Wu, Xiaojing; Gajdos, Fruzsina; Heck, Alexander; de la Lande, Aurélien; Blumberger, Jochen; Elstner, Marcus, *RCTF 2016*, Lyon France (July 2016).
**Computational Chemistry Tools for Biological Electron Transfers**
Gillet, Natacha*; Elstner, *Marcus Network Meeting of the Alexander von Humboldt Foundation*¸ Düsseldorf Germany (March 2016)
**Electron and Hydrogen Atom Transfers in the Hydride Carrier Protein EmoB**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; de la Lande, Aurélien *TYC Enzyme Catalysis Workshop,* London UK (June 2014)
**TTQ redox potential in MADH protein: a QM +MM study**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; de la Lande, Aurélien *Cecam Workshop: Investigating fine quantum effects in biological systems: toward a synergy between experimental and theoretical approaches?* Paris France (May 2014)
**TTQ redox potential: reaching the best balance between configurational sampling and electronic description.**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; de la Lande, Aurélien *13eme journées francophones des jeunes physico-chimistes*, Dinard France (October 2012)
**Steptwise vs. sequential mechanism of hydride transfers between flavins: a constrained DFT and ELF analysis study.**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; Piquemal, Jean-Philip; de la Lande, Aurélien *Xth Girona Seminar on Theoretical and Computational Chemistry for the Modeling of Biochemical Systems* , Girona, Spain (July 2012)
**TTQ redox potential: reaching the best balance between configurational sampling and electronic description.**
Gillet, Natacha*; Demachy, Isabelle; Moliner, Vicent; Lévy, Bernard; de la Lande, Aurélien *8th Congress on Electronic Structure: Principles and Applications.* , Barcelone, Spain (July, 2012)

## ANNEX A : THESIS ABSTRACT

During my PhD, I was interested by electron transfers in proteins involving organic cofactors with a particular care paid to the balance between quality of the electronic description and of conformational sampling. The main idea was to study three different proteins with different problematic:

i) evaluation of the redox potentials quinone derivatives in MADH protein. This study firstly focus on force field parameterization of the cofactor (see **article 7**), followed by test of different QM/MM and QM+MM approaches in water solution. A calibration curve of our results *vs* experiments has been determined. Application to MADH and MADH/amycianin complex was tested using classical molecular dynamic.

ii) mechanistic description of the L-lactate oxidation into pyruvate in the flavocytochrome $b_2$ enzyme in collaboration with Dr. Lederer (for experiment). A QM(AM1)/MM scheme was used to determined free-energy surface of the reaction combining a proton and a formal hydride transfer. Influence of the environment was studied by applying different mutations (see **article 2**)

iii) decomposition of the formal hydride transfer into hydrogen and electron transfers occurring between two flavins in EmoB protein. Constrained DFT was used to fix the electron on each flavin for different positions of the hydrogen atom. Hundreds of nanoseconds were simulated to determine the role of the environment on the charge transfer: flavins force field parameters were determined thanks to constrained DFT/MM calculation and constrained DFT/MM energies were calculated along the classical molecular dynamic simulation. (see **article 6**)

To complete my acknowledge about numerical simulations, I spent one month to the Department of Physics of the Freie Universität of Berlin under the supervision of Petra Imhof in order to study the thymine release from thymine DNA glycosylase using classical simulations and adaptive biasing forces calculations.

**Skills:** classical and QM/MM simulations, force field parameterization, free energy calculation (umbrella sampling, free energy perturbation, free energy integration, adaptive biasing forces), DFT, constrained DTF, semi-empirical approaches. Collaboration with experimentalist

## ANNEX B : POSTDOC ABSTRACT

Involved in the development of biological charge transfer simulations in the group of Pr. Elstner, I am working on different projects:

i) test of different QM approaches to determine electronic coupling for charge transfer in organic and bioorganic systems (peptides, protein and DNA) (see **article 1**). This work is in collaboration with Dr. Berstis (USA), Pr. Blumberger (UK) and Dr. de la Lande (France)

ii) study of different photolyases proteins in collaboration with Pr. Lamparter group (experimental group). Charge transfer simulations (DFTB/MM), protonation steps (DFTB/MM), interaction with DNA (modeling of the interaction and dissociation constant calculations at classical level), impact of mutations, comparison between different protein of the cryptochromes and photolyase family, parameterization at DFTB and classical level of $Fe_4S_4$ cluster (possible international collaboration). PhD project of Daniel Holub.

iii) Electron transfer in azurin protein involving DFTB/MM code development.

iv) Charge transfer in ribonucleotide reductase with long classical MDs (1µs + several hundreds nanoseconds MD) and proton coupled electron transfer code development and simulations (direct simulation and free energy calculations)

**Skills:** classical and DFTB/MM simulations, force field and DFTB parameterization, programing, project submission and supervision, PhD supervision, international collaborations and collaborations with experimental groups.

## ANNEX C : TEACHING

During my PhD, I taught two year in chemistry at the Science faculty of Université Paris Sud (now Paris Saclay):

- lectures and tutorials in atomistic (L1): introduction to the quantum chemistry (atomic spectra, Time-independent Schrödinger equation, hydrogen atoms, atomic orbitals, molecular orbital of diatomic molecules, orbital diagram), atoms and molecular properties (electronegativity, partial charges, geometry: VSEPR). 22 hours lectures (2 years) + 20 hours tutorials (1 year)

- practicals in solution chemistry (L2). Chemical dosages (spectrometry, pH, conductivity). 14 hours (1 year)

- tutorials in inorganic chemistry (Master 1): exercises related to the inorganic chemistry lecture. Metallic complex study: geometries, d orbital diagram, crystal and ligand field theory, electron transfers. 12 hours (2 years)

- Practicals in statistical thermodynamics (Master 1- Magister): simulation of argon cluster or zeolithes in different thermodynamic ensembles. Small simulations and analysis using xmgrace. 8-16 hours (2 years).

- Practicals in computational biochemistry (Master 2): study of electron transfer with classical MDs using VMD and electron pathway model. 3 hours (2 years)

## ANNEX D: POPULARIZATION OF SCIENCE

During my L3 year, I participated to science workshop in primary schools on different subjects: water, chemistry in food and for different level: CP, CE2 and CM1/CM2. This required preparation of different experiments for children and teaching during several sessions in collaboration with teachers and “la maison des sciences” à Chatenay-Malabry.

During my PhD, I went back to “la maison des sciences” to prepare an exhibition for children about Pasteur. This exhibition mixed experiments, games, posters and website (https://sites.google.com/site/surlestracesdepasteur/) about different aspects of Pasteur work: crystallography and chirality, fermentation, silkworm diseases, hygiene and vaccines. The final exhibition was presented to children and teacher from abroad and it is available for every school asking for it. A formation for high school teachers was also given about Pasteur and his work.

Finally, I participated to the l’Oréal program for Girls in science, presenting during one hour my work and the possibilities of scientific careers to high school pupils.