Dr. Claudia Clopath

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EDUCATION

2011 - present	**Columbia University** (USA) Postdoc (independent position)
2009 - 2011	**Universite Paris Descartes** (France) Postdoc (with Nicolas Brunel) Cerebellar learning
2005 - 2009	**EPFL** (Switzerland) PhD (advisor - Wulfram Gerstner) Synaptic plasticity across different time scales and its functional implications
2008	**Freiburg University** (Germany) Advanced Course in Computational Neuroscience
2004 - 2005	**MIT** (USA) Master thesis (advisor - Martha Gray) Study of cartilage biosynthesis using magnetic resonance spectroscopy
2002 - 2003	**University of Waterloo** (Canada) Exchange year in Physics
2000 - 2005	**EPFL** (Switzerland) BA & MA in Physics

GRADES AND AWARDS

2010	Vasco Sanz Prize (Swiss Neuroscience Prize)
2005	Grade for the Master thesis: 6/6
2005	Final grade of the Master: 5.62/6
2000	Physics and Mathematics award in high school, Nyon

TEACHING EXPERIENCE

2012	Tutor in Okinawa Computational Neuroscience Course
2012	Workshop on Mathematical Neuroscience, Edinburgh (UK) Invited lecturer
2011	Tutor in Okinawa Computational Neuroscience Course
2010	1st Baltic Autumn School, Lübeck (Germany) Invited lecturer
2009 - present	Supervision of PhD and Mater students

2009 - 2010	Teaching at Université Pierre et Marie Curie, Paris (France) Réseaux neuronaux : traitement et représentation de l'information
2005 - 2009	Teaching assistant at EPFL (Switzerland) Computational Neuroscience course

SKILLS

Languages	Fluent in French, German, English
Programming	Matlab, Python, HTML
Tools	Eclipse, LaTeX, Illustrator

REVIEWING ACTIVITY

Journals	Nature Neuroscience Biological Cybernetics PLoS Computational Biology Neural Computation Frontiers in Neuroscience Journal of Physiology - Paris Journal of Mathematical Neuroscience
Conferences	Annual Computational Neuroscience Meeting (CNS)

PUBLICATIONS

[iii] Clopath C, de Zeuuw C, Brunel N.
Model of Vestibulo-Ocular Reflex learning – Role of delay in Climbing fibers
In preparation

[ii] Clopath C, Brunel N.
Maximal capacity and weight distribution of a linear perceptron as a Purkinje cell model
In preparation

[i] Clopath C
STDP with homeostasis computes Independent Component Analysis
In preparation

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[10] Clopath C, Brunel N.
Storage of correlated patterns in standard and bistable Purkinje cell models
Accepted in PLoS Computational Biology

[9] Vogels TP, Sprekeler H, Zenke F,Clopath C, Gerstner W.
Inhibitory Plasticity Balances Excitation and Inhibition in Sensory Pathways and Memory Networks
Science, 334(6062),1569-1573,2011

[8] Gjorgjieva J, Clopath C, Audet J, Pfister J-P.
A triplet spike-timing–dependent plasticity model generalizes the Bienenstock–Cooper–Munro rule to higher-order spatiotemporal correlations
PNAS, 108 (48), 19097-19098, 2011

[7] Clopath C
Synaptic Consolidation. An approach to long-term learning.
Cognitive Neurodynamics, 1-7, 2011

[6] Clopath C, Gerstner W.
Voltage and Spike Timing interact in STDP - a Unified Model
Frontiers in Synaptic Neuroscience, doi:10.3389/fnsyn.2010.00025, 2010

[5] Clopath C, Vasilaki E, Büsing L and Gerstner W.
Connectivity reflects coding: A model of voltage-based spike-timing-dependent-plasticity with homeostasis
Nature Neuroscience, 13, 344-352, 2010

[4] Clopath C, Ziegler L, Vasilaki E, Büsing L and Gerstner W.
Tag-Trigger-Consolidation: A model of early and late long-term potentiation and depression
PLoS Computational Biology, 4, e1000248, 2008

[3] Clopath C, Longtin A and Gerstner W.
An online Hebbian learning rule that performs Independent Component Analysis
Advances in Neural Information Processing Systems 20, MIT Press, 312-328, 2008

[2] Naud R, Marcille N, Clopath C, Gerstner W.
Firing Patterns in the Adaptive Exponential Integrate-and-Fire
Biological Cybernetics, 98:459-478, 2008

[1] Clopath C, Jolivet R, Rauch A, Lüscher H-R and Gerstner W.
Predicting Neuronal Activity with Simple Models of the Threshold Type: Adaptive Exponential Integrate-and-Fire Model with Two Compartments
Neurocomputing, 70, 1668 – 1673, 2007

THESES

[b] Clopath C.
Synaptic plasticity across different time scales and its functional implications
PhD Thesis, EPFL, no 4498, 2009

[a] Clopath C.
Study of cartilage biosynthesis using magnetic resonance spectroscopy
Master Thesis, EPFL & MIT, 2005

TALKS

Invited at Workshop on **Mathematical Challenges in Neural Network Dynamics**, Mathematical Biosciences Institute, Oct 2012.
Modeling synaptic plasticity.

Invited at **Mathematical Neuroscience** conference, Edinburgh, Ma 2012.
Storage of correlated patterns in binary Purkinje cell models.

Invited at Workshop on **Learning and Plasticity**, Marseille, Nov 2011.
Storage of correlated patterns in binary Purkinje cell models.

Cosyne, Salt Lake City, Ma 2011.
A combined model of the induction and the consolidation of synaptic plasticity.

Invited at **Kleinfeld's Lab, UCSD,** San Diego, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

Invited at **Sejnowski's Lab, Salk Institute**, San Diego, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

Invited at the **Redwood Center, Berkeley**, San Francisco, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

Invited at **Frank's Lab, UCSF**, San Francisco, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

Invited at **Sur's Lab, MIT**, Boston, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

Invited at **Moore's Lab, MIT**, Boston, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

Invited at **DiCarlo's Lab, MIT**, Boston, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

Invited at **NIPS** workshop on "Activity-Dependent Plasticity", Vancouver, Dec 2010.
Why is connectivity in barrel cortex different from that in visual cortex? - A plasticity model.

1st Baltic Autumn School, Lübeck, Sep 2010.
Frequency and Spike-Timing dependent Plasticity interact in a Recurrent Network.

1st Baltic Autumn School, Lübeck, Sep 2010.
Model of Synaptic tagging.

9th Computational Neuroscience Day, Paris, Sep 2010.
Frequency and Spike-Timing dependent Plasticity interact in a Recurrent Network.

Invited at **IDSIA**, Lugano, Aug 2010.
How supervised learning can teach you about neural code?

Invited at the **Group for Neural Theory**, **ENS**, Paris, Apr 2010.
Connectivity reflects coding: a voltage based STDP rule.

Facets, Dresden, Jan 2010.
Connectivity reflects coding: a voltage based STDP rule.

Invited at **Martin Nawrot's lab**, BCCN, Berlin, May 2009.
Modeling synaptic plasticity across different time scales: LTP induction and consolidation.

SSN, Fribourg, March 2009.
Modeling synaptic plasticity across different time scales: the influence of voltage, spike timing, and protein synthesis.

Invited at the **Center for Theoretical Neuroscience, Columbia U.**, New York City, Feb 2009.
Modeling synaptic plasticity across different time scales: LTP/LTD induction and consolidation.

BMI-EPFL retreat, Villars, Feb 2009.
Modeling synaptic plasticity across different time scales: LTP induction and consolidation.

Facets, Lausanne, Oct 2008.
Modeling induction of LTP/LTD: the role of voltage and spike timing.

Advanced Course in Computational Neuroscience, Freiburg, Aug 2008.
Effect of lateral connections in a plastic mainly feed-forward network.

SIAM, Montreal, Aug 2008.
A unified voltage-based model for timing and voltage dependent synaptic plasticity.

CNS, Portland, Jul 2008.
An online Hebbian learning rule that performs Independent Component Analysis.

Cosyne, Salt Lake City, Ma 2008.
Voltage model of STDP leads to BCM and ABS.

Facets, Debrecen, Feb 2008.
Modeling Synaptic Plasticity.

Invited at **André Longtin's lab**, **U. Ottawa**, Ottawa, Dec 2007.
An online Hebbian learning rule that performs Independent Component Analysis.

Conferences and Workshops Organization

Cosyne 2011 Workshops	"Synaptic plasticity across multiple time scales"
SFN 2011 conference	Computational Neuroscience Social

Funding

2012-2013	SNSF (Switzerland), Fellowship 109,000$ for two years
2011-2012	Swartz Foundation, Postdoc salary
2010	Qualcomm travel grant for Cosyne conference

References

Prof. Wulfram Gerstner	Professor at EPFL (Switzerland) +41216936713, wulfram.gerstner@epfl.ch PhD advisor
Dr. Nicolas Brunel	CNRS researcher at U. Paris Descartes (France) +33149279062, nicolas.brunel@parisdescartes.fr Postdoc director
Dr. Eleni Vasilaki	Lecturer at Sheffield University (UK) e.vasilaki@sheffield.ac.uk Collaborator

Extracurricular Activities

Sports trainer for disabled people, Plusport, Switzerland

Blood donation assistant for the Red Cross, Nyon, Switzerland

Soupe Populaire (food distribution for people in need), Lausanne, Switzerland

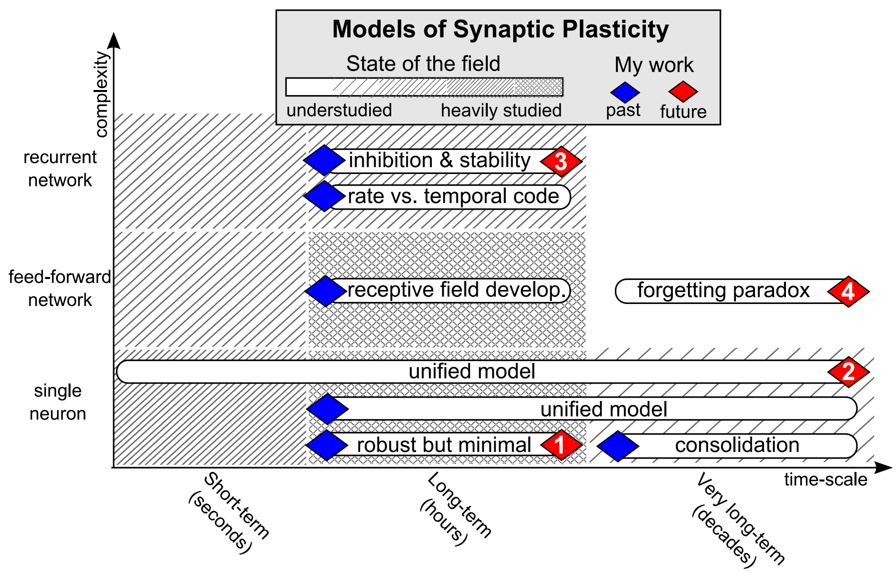
Tango, traveling, swimming, mountain climbing, skiing, squash

Statement of Research Objectives

Executive Summary

Animals have the fascinating ability to ***learn*** to adapt to their environment, as well as ***memorize*** experiences. While little is understood about the underlying mechanisms and their development as of yet, emerging experimental techniques are opening new avenues of research – especially on the intermediate scale of complexity between single cells and entire brains. A crucial role in this endeavor falls to ***computational modeling***, which is complementary to experiments: it permits the study of neuron assemblies of any size, where, unlike in biological experiments, every feature can be manipulated independently. Ideally, theoretical and modeling results inspire new experiments which in turn trigger further theoretical advances.

My core research interest lies in ***synaptic plasticity***, that is, how the strength of synapses between neurons changes, which is believed to be the key neural mechanism involved in learning and memory. My past research focused on two levels: ***Modeling*** synaptic plasticity in order to explain the phenomenology and studying its ***role and function*** in the development of networks. More precisely, I designed models of plasticity for the long-term (hours) and very long-term (years), and built plastic artificial neuronal networks that can explain different types of information coding in different brain areas.



In the future, I intend to both expand upon my pioneering work, and claim some hitherto uncharted ground. I will design ***models of long-term plasticity*** ***(1)*** that are detailed enough to reproduce crucial features of biology but compact enough to be of use in networks. Synaptic plasticity varies with time scale, but models are only designed for a single one; worse, models of very long-term plasticity were completely neglected before my work. I therefore intend to build ***a unifying model across all three time scales*** ***(2)***, just like I unified long-term and very long-term. On a more functional level, I will build ***spiking plastic recurrent networks*** ***(3)***, to study the effect of recurrence and inhibition, as well as the balance between inhibition and excitation over the development of an animal. Animals are capable to learn quickly and remember for a long time, so synapses should be highly plastic for memory encoding but less plastic during retrieval – I believe that my model of very long-term plasticity might solve this paradox: I will investigate how the amount of stored information relates to the ***lifetime*** of these ***memories*** in ***very long-term plastic recurrent networks*** ***(4)***, possibly establishing at the same time how memory consolidation depends on the developmental phase.

The Field: Computational Modeling of Learning and Memory

Animals and humans have the fascinating ability to ***learn*** to adapt to their environment, ***memorize*** experiences, and those abilities develop during their life. While little is understood about the underlying mechanisms as of yet, emerging experimental techniques are opening new avenues of research – especially on the intermediate scale of complexity between single cells and entire brains. Many approaches, such as behavioral neuroscience, genetics and physiology, complement each other in this endeavor, but a crucial role falls to ***computational modeling***: it permits the study of neuron assemblies of any size, where, unlike in biological experiments, every feature can be manipulated independently. Mathematical models and computer simulations allow experimental hypotheses to be confirmed, and can propose new predictions to be tested experimentally. Ideally, outcomes of these experiments trigger further theoretical advances, thus closing the circle. Among computational modeling's great past successes is the discovery of ***Spike-Timing Dependent Plasticity*** (STDP, i.e. synaptic plasticity dependent on the precise timing of the pre- and postsynaptic spike time)[1], predicted before the first experimental evidence. The computational modeling approach is especially powerful, even more so than for single-neuron models, for studying learning, memory and development in ***networks of neurons*** (and eventually whole brain areas), for which reliable experimental measures are notoriously difficult to achieve. If, as is the current consensus opinion, memory is stored in the strength of synapses, it can be studied in the form of neural learning rules within large, recurrent networks, which are eminently suited for a computational approach.

My Previous and Current Research

I am broadly interested in the field of neuroscience, especially insofar as it addresses the questions of development, ***learning*** and ***memory***. During my Ph.D. in Prof. Wulfram Gerstner's lab, I modeled synaptic plasticity across different time scales, and developed models of long-term plasticity that use the appropriate types of neuron models[2,3], which reproduce slice experiments in a number of different systems (hippocampus, visual cortex, somatosensory cortex)[4-6]. I pioneered the previously ignored modeling of ***very long-term plasticity*** (memory over whole lifespans), that is, the mechanism of ***synapse consolidation***[4]. I also established the first connection between plasticity on this very long-term timescale and long-term plasticity (hour-long memory).

My work on the functional implications of plastic networks is twofold. First, in feed-forward networks, I studied the role of synaptic plasticity in ***receptive field development*** and how plasticity shapes selectivity in the inputs[5]. I proposed a mechanism of how learning can develop ***orientation selectivity*** in visual cortex[5] and perform ***blind source separation*** (e.g. demixing sounds at a cocktail party)[7]. Second, for recurrent networks, I proposed a new model that, for the first time, explains the close relation between the ***type of coding*** and the ***type of connectivity*** found in different brain areas[5]. Among others, this could explain the recently observed differences between the neural code in visual cortex and in barrel cortex. Those results and predictions have been highly influential; my Nature Neuroscience article triggered 15 citations in just 6 months, and generated a whole set of new experimental questions.

My post-doctoral work is related to ***cerebellar learning***, where I am studying how ***optimal memory capacity*** can predict synaptic weight distributions between Parallel Fibers and Purkinje Cells [accepted][8]. Further, I am modeling a learning task from in vivo recordings of the Vestibulo-ocular reflex [in prep.][9], to determine the ***impact of the teaching signal*** (Climbing Fiber) on learning. My newest project is a collaboration with Tim Vogels, where we study the ***balance between inhibition and excitation*** across development [accepted in Science].

My Future Research

My future research plans consist in four projects in the following two directions: developing models of synaptic plasticity (1 and 2), and studying the functional implications of plasticity in networks (3 and 4). Two of these projects (1 and 3) are extensions of my current work and are likely to succeed, and the other two (2 and 4) are genuinely novel approaches that could lead to breakthrough results.

1) Modeling Long-term Plasticity

Existing models of synaptic plasticity tend to be either over-simplified or too detailed. I want to pursue my research in designing models that bridge this gap: discovering functional implications requires the underlying models to be at once compact enough to employ within large networks, and rich enough to describe critical biological features (such as the dependency on neuromodulators like dopamine).

In order to understand the mechanism and the role of plasticity, it is important to build a model of synaptic plasticity that addresses the dependencies on all the features shown experimentally. During the 15 years since the discovery of Spike-Timing Dependent Plasticity (STDP), that is, the dependence of synaptic plasticity on the precise timing between the pre- and the postsynaptic spike, modeling has been focused mostly on this property. However, as I showed in my Nat. Neursci. paper[5], accounting for the nonlinearities in spike interactions have dramatic consequences on the behavior of recurrent networks.

The duty of the modelers is to provide the right tradeoff between compactness and robustness in their models, so that the models can then be used by the larger neuroscience community for emulating plastic networks with VLSI hardware[10] or simulating large-scale networks (see project 3, below). My goal is therefore to extent models of long-term synaptic plasticity to take into account

- i) the dependency of the synaptic weight change on the ***actual weight*** [11-13],
- ii) the non-linearity in the ***number of pairings*** and the ***saturation effects***[14],
- iii) the dependence on synaptic ***location on the dendrites***[15,16],
- iv) the ***influence of neuromodulators.*** Neuromodulatory systems act on plasticity via dopaminergic, muscarinic, noradrenergic, and nicotinic receptors. Recent experimental findings that define the conditions by which plasticity induction is enabled[17-25] await being incorporated in models. A model of modulated plasticity will be linked to ***reward learning*** and give insights into behavior learning.

These types of models are so-called biophysical or phenomenological; they are directly inspired by experimental data (bottom-up). Given my additional expertise in developing top-down models[7], designed to perform a certain function, I intend to bring those two types of models together. For example, ***receptive field development***[26,27] and ***reinforcement learning***[28,29] are both currently addressed by a top-down and an orthogonal bottom-up approach, missing a unifying view.

2) Synaptic Plasticity across Different Time-scales

I want to unify the models of the 3 different memory timescales (short-, long-, very long-term). The most challenging aspect is determining how learning on different timescales interacts. Such a unified view might lead us to reconsider and adapt some well established but isolated models.

Each year, short-term plasticity[30], long-term plasticity[31] and very-long term plasticity[32] are better understood, due to the increasing amount of experimental data and theoretical models. Much less is known about the way they could ***interact***, however, and whether there are computational advantages to such a ***wide range of time-scales***. Being the first to develop a model of the very long-term of plasticity and its interaction with the long-term[4], I am thus well placed to design a model that incorporates all the time scales.

As a kick-off meeting, I ***organized a workshop at Cosyne*** in February 2011, in order to bring together key experimentalists and theoreticians to discuss precisely how different time scales of synaptic plasticity can be combined. This workshop attempted to define the urgent questions to be addressed, which models should be reconsidered, and initiate collaborations between the top people in the field.

3) Functional Implications of Long-term Plasticity

Computational modeling permits establishing links between neural properties and behavior, beyond what biological experiments can currently provide. I will continue my work in this field, in particular insofar as it pertains to the understudied type of recurrent networks: no existing plastic model accurately describes networks where the recurrent dynamics dominate, nor how inhibitory and excitatory plasticity influence stability.

One of the ultimate goals of neuroscience is to understand our behavior. The challenge lies in establishing links between neural properties and high-level functions. At the current state of technology, directly measuring these links in biology is often undoable, despite new techniques such as imaging[33] and optogenetics[34] which are suited to the study of neural dynamics. Computational modeling is therefore crucial in this domain, especially when experimentalists and theoreticians work hand in hand.

Plastic feed-forward networks are fairly well characterized[26]. However, few people have studied plastic ***recurrent networks*** with spiking neurons[35,36,5]. Seeing how my Nature Neuroscience paper, which opened up new such perspectives, has been cited over 50 times in just one year since publication, it appears that the topic is generating momentum. One of the most interesting extensions in my eyes would be to use the model in large-scale networks with strong recurrent connections, which could shed light on the mechanism that permits ***information flows*** within networks[37]. Another striking gap to our knowledge that I plan to address concerns ***inhibitory***

plasticity[38-41] in recurrent networks, thereby allowing the study of the balance between ***excitation and inhibition*** across development, as shown in our recent Science paper. I intend to study the interplay between excitatory and inhibitory plasticity in order to understand how they interact and how does it affect memory encoding versus stability.

4) Functional Implications of the Late-phase of Plasticity

We know that humans can both learn very quickly and remember for very long. On the synaptic level, those two functions seem difficult to combine, as a synapse should both be highly plastic when learning quickly but not too plastic to avoid forgetting[45,46]*. I believe the model of very long-term plasticity I developed might offer a solution to this dilemma. I intend to investigate its memory storage capacity in a network, as well as the stability of memories once formed.*

Behavioral correlates of very long-term synaptic plasticity have been shown experimentally[47,48]. I plan to investigate the properties of my model of very long-term plasticity (also known as consolidation) under conditions similar to those behavioral experiments. After thus confirming its plausibility, I will move on to study the role of consolidation in ***recurrent networks***. The questions of interest here are which topologies the final weight distributions infer, as well as whether consolidation can help to ***increase memory capacity or memory life-time***. I am interested in studying ***associative memories*** using a Hopfield-type network with the consolidation mechanism[49], which could be seen as a two level cascade model[50] designed to increase memory lifetime and therefore analyzable using the same theoretical framework[50].

My Role in the Department of Neuroscience at Brown University

As my curriculum vitae shows, I have collaborated with a broad range of people, both theoreticians and experimentalists. I am sure that being an assistant professor would be an even greater opportunity for me to collaborate with PIs in the Neuroscience Department, such as Profs Julie Kauer, Christopher Moore, Rebecca Burwell, Jerome Sanes and Diane Lipscombe also interested in learning and memory and with Profs Lucien Elie Bienenstock and Leon Cooper with whom I could share similar theoretical and computational tools.

References

1. Gerstner, W., Kempter, R., Hemmen, J.L.V. & Wagner, H. A neuronal learning rule for sub-millisecond temporal coding. *Nature* **383**, 76-78 (1996).
2. Clopath, C., Jolivet, R., Rauch, A., Luescher, H. & Gerstner, W. Predicting Neuronal Activity with Simple Models of the Threshold Type: Adaptive Exponential Integrate-and-Fire Model with Two Compartments. *Neurocomputing* **70**, 1668 - 1673 (2007).
3. Naud, R., Marcille, N., Clopath, C. & Gerstner, W. Firing patterns in the adaptive exponential integrate-and-fire model. *Biological Cybernetics* **99**, 335-347 (2008).
4. Clopath, C., Ziegler, L., Vasilaki, E., Buesing, L. & Gerstner, W. Tag-Trigger-Consolidation: A Model of Early and Late Long-Term-Potentiation and Depression. *PLoS Comput Biol* **4**, (2008).
5. Clopath, C., Büsing, L., Vasilaki, E. & Gerstner, W. Connectivity reflects Coding: A Model of Voltage-based Spike-Timing-Dependent-Plasticity with Homeostasis. *Nature Neuroscience* **13**, 344 - 352 (2010).
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Teaching Interests and Record

I have accumulated a broad range of teaching experience, with several years of teaching assistantship (computational neuroscience), and classes I taught at university (neuroscience modeling) and an autumn school (computational neuroscience and neuroengineering). In addition, I supervised two Master students and one PhD student, and had ample opportunity to perfect my oratory skills, being invited to give talks at many different labs and conferences, e.g. Cosyne, SIAM, NIPS or CNS. I am looking forward to apply my teaching skills to the students of Brown University.

With my background in Physics and my expertise in computational methods, I am able to offer a variety of specific classes on top of the basic courses. I am listing below a collection of courses I would be interested in teaching, ordered from advanced classes (for PhD or MA students) to more basic classes (for BA students). I am of course willing to teach other classes as well.

Teaching Proposition

- ***Computational neuroscience***: Single neuron models, synaptic plasticity, network, coding, learning.
- ***Computer simulators*** for detailed neuron models and neuron networks: NEST, NEURON, BRIAN.
- ***Machine learning***: Bayesian methods, support vector machines, artificial neural networks, reinforcement learning.
- ***Statistics and data analysis***: Introduction to statistics and probability, permutation test, bootstrap methods, Monte-Carlo simulation, T-test, multivariate statistics, analysis of variance, maximum likelihood estimation, Bayesian approach.
- ***Physics*** and its relevance for biology, e.g., electromagnetism.
- ***Programming*** basics: Matlab, Python.

Teaching Experience

- Tutor in Okinawa Computational Neuroscience Course 2012
- Tutorial for the Mathematical Neuroscience Conference, Edinburgh (UK) 2012
- Tutor in Okinawa Computational Neuroscience Course 2011
- Invited lecturer at 1st Baltic Autumn School, Lübeck (Germany) 2010
- Supervision of PhD and Mater students 2009 – now
- Teaching at Université Pierre et Marie Curie, Paris (France) 2009 – 2010
  Réseaux neuronaux : traitement et représentation de l'information
- Teaching assistant at EPFL (Switzerland)
  Computational Neuroscience course 2005 - 2009