Chiara Fornari, Ph.D.

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Mathematical Neuro-Oncology
Laboratory
September 23, 2014

Northwestern University
Feinberg School of Medicine
Chicago, IL
USA

Dear Dr. Rockne,

I am Chiara Fornari, and I am a postdoctoral fellow at Departments of Computer Science and of Molecular Biotechnology and Health, of the University of Torino (Italy).
I met Dr. Swanson last year in Carmona (Spain) during the conference "Mathways Into Cancer II", when I was really impressed by the work she presented, and by how the models she developed were so realistic, predictive, and useful for the bio-medical community. At that time I was a graduate student, dreaming about the possibility of working in such a type of interdisciplinary, stimulating, and scientific team. I am currently looking for a postdoctoral position, and I think that the scientific activities of the Mathematical Neuro-Oncology lab perfectly match my research interests, so that I feel eager to be part of it. Therefore, this email is to inquire about the possibility of joining Dr. Swanson's laboratory.

My background is in applied mathematics (mostly in numerical methods and differential equations) and, for my doctoral studies, I moved into the interdisciplinary field of Computational and Mathematical Oncology, working under the supervision of Prof. Balbo (Department of Computer Science), prof. Calogero (Department of Molecular Biotechnology and Health), and Prof. Tyson (Department of Biology, Virginia Tech, Balcksburg, USA). Through these experiences I developed the ability of combining formal mathematical approaches with the capability of communicating with scientists from different fields.

My research interests concern Systems Biology, Mathematical Oncology, and specific mathematical formalisms, such as Differential Equations (DEs) and Petri Nets (PNs). In particular, I work on mathematical models describing tumor development, with a specific interest for those tumors characterized by the Cancer Stem Cell (CSC) hierarchy. I take into account different aspects of cancer growth, such as molecular networks and population dynamics, thus considering the different scale phenomena involved in tumor development. For this purpose I use different mathematical formalisms, such as DEs and PNs, depending on the specific problem under investigation. Briefly, I have worked on the following main topics: (i) multi-level modeling, (ii) data/model integration, and (iii) model parameter analysis.
More in details, I described ErbB2-carcinogenesis through a multi-level model based on the inter-dependencies between cell population dynamics and molecular events [Cordero et al., BMC Bioinformatics, 2013]. Later on, I expanded the study of population dynamics defining a compartmental model reproducing CSC hierar-

chy. Biological data were integrated in this framework, which was then used to explain different scenarios of cancer progression with respect to mutual CSC and non-CSC variation, and to investigate some targets of cell markers [Fornari et al., PLOS One, 2014].

Afterwards, I refined this model with internal controls of tumor cell number introducing some feedback regulatory mechanisms governing cell self-renewal. This new model helped to characterize the role of CSC symmetric proliferation as a discriminating factor of the tumor outcomes [Fornari et al., BMC Bioinformatics, under revision]. More recently, in addition to cancer dynamics, I have been interested also in general issues related to modeling, such as parameter analysis. In particular, I recently designed a pipeline suitable to characterize ODE system behaviors and to identify those parameters influencing such dynamics [Fornari et al., BMC Bioinformatics, under revision].

In the future, I would like to continue my research on Mathematical Oncology, expanding my studies on multilevel and multiscale models, which are very versatile tools that can be tailored for different scenarios. I would like to join a team which builds realistic models that help to gain a deep understanding of cancer biology, and the patient-specific models developed in Dr. Swanson's lab perfectly represent this type of tools. I am enthusiastic about the possibility of being engaged in different research projects involving the application of mathematical models, and to work in a true integrated and collaborative environment where theoretical approaches and experimental studies are combined. I also find very stimulating the possibility of following the whole modeling process, step by step: from data acquisition, through model creation, to hypotheses generation. Moreover, I would like also to enhance my skills in modeling applying new tools such as image analysis techniques and methods to integrate patient-specific data. Given the high expertise that Dr. Swanson's lab has in all these aspects, and that it is at the forefront of the Mathematical Oncology field, I feel eager to be part of it. Lastly, I am excited about the idea of moving abroad to work in an international and dynamic context, as I did for some months during my Ph.D. studies.

For all these reasons I consider working in Dr. Swanson's laboratory, and being in close contact with the scientific community of the Brain Tumor Institute, a crucial and challenging opportunity to improve my expertise in Mathematical Oncology field and to contribute to the Cancer Research. I kindly request you to evaluate my application and I thank you for your time and consideration. I very much look forward to the possibility of speaking with you about my interest in joining Dr. Swanson's lab.

Yours sincerely,

Chiara Fornari
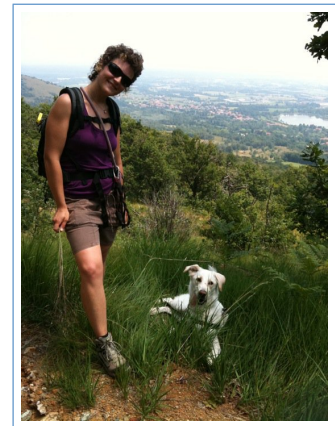

Enclosure Attachment: curriculum vitæ

Chiara Fornari

curriculum vitae

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RESEARCH INTERESTS

○ Computational Biology
○ Mathematical Oncology

RESEARCH SUMMARY

My field of research is Mathematical Oncology, i.e. the study of cancer through the application of mathematical models. More precisely, I work on a specific set of tumors whose growth and progression are influenced by a small subpopulation of cancer cells, known as Cancer Stem Cells (CSCs).

In these studies, CSC-tumor growth has been described considering two main aspects: (i) dynamics occurring among the different subpopulations of cells, as detailed by CSC theory; and (ii) regulatory networks describing key cellular events in tumorigenesis as, for instance, proliferation. Models are built with different mathematical formalisms, such as Differential Equations (DEs) and Petri Nets (PNs) [J3]. In particular, I used both formalisms to define a multi-level model of ErbB2-carcinogenesis in which both molecular and cellular aspects were considered. This framework describes the interplay between ErbB molecular pathways controlling cell proliferation (level one) and the inter-dependencies among the different tumor cell subpopulations (level two) [J4].

Later on, I expanded the study on cell subpopulation dynamics defining a compartmental DE model on the initial phase of CSC-tumor progression [J2]. *In vitro* and *in vivo* data were integrated in the model to reproduce dynamics of breast cancer growth observed in mice. This CSC-model was used to characterize the distinct scenarios of cancer progression with respect to mutual CSC and non-CSC variation, and to investigate some targets of cell markers.

Afterwards, I further extended this model to describe CSC-based tumor in all tumorigenesis phases. More precisely, an internal control of tumor cell number was introduced defining feedback regulatory mechanisms governing cell self-renewal [J1]. Model predictions helped to characterize the role of CSC symmetric proliferation as discriminating factor between tumorigenesis and unsustainable tumor growth. More recently I have become also interested in general issues related to modeling, such as parameter analysis. In particular, I worked on a pipeline that helps to characterize ODE system behaviors and to identify those parameters influencing such behaviors. This tool is based on statistical methods and it is useful to determine relationships between input parameters and model output values [J1].

Research Activity

Jan 2014
Present
Research fellowship, *Department of Computer Science, Department of Molecular Biotechnology and Health Sciences, University of Torino*,
Supervisors: dr. Francesca Cordero, prof. Raffaele A. Calogero, prof. Gianfranco Balbo.

Sep 2012
May 2013
Visiting scholar, *Department of Biological Sciences, Virginia Tech*, Blacksburg, VA, USA,
Supervisor: prof. John J. Tyson.

Sep 2009
Dec 2010
Researcher, *Acusidea, Lagrange Project: "The challenge of the complexity"*, Torino,
Project: Clustering Analysis on the market of muliutilities
Supervisors: dr. Paola Ponzo (Acusidea), prof. Paolo Brandimarte (Politecnico di Torino) and prof. Giulio Zotteri (Politecnico di Torino).
I awarded a scholarship within the Lagrange Project, which was founded by Cassa di Risparmio di Torino (CRT) and Institute for Scientific Interchange (ISI) foundation. The aim of the project was the creation of a tool to cluster the Italian electricity market considering clients' behaviors. I worked on this project at Acusidea, a company providing consulting technology services.

Education

Jan 2014
PhD in Complex Systems in Medicine and Life Sciences, *University of Torino*,
Thesis: Mathematical models on cancer progression
Supervisors: dr. Francesca Cordero, prof. Raffaele A. Calogero, prof. Gianfranco Balbo.

Mar 2009
Master degree in Mathematics, *"summa cum laude"*, *University of Torino*,
Thesis: Multivariate scattered data interpolation using a class of radial basis function with a local support
Supervisor: prof. Giampietro Allasia.

Dec 2006
Bachelor degree in Mathematics, *105/110*, *University of Torino*,
Thesis: Iterative methods for linear systems
Supervisor: prof. Alessandra De Rossi.

Skills

Language Skills
Italian: native proficiency
English: full professional proficency

Computing Skills
Software for Modeling: Matlab, Mathematica, Maple
Programming Languages: R, Pl-Sql, C++
Operating Systems: Linux, Windows

Teaching Activity

A.Y. 2011/2012
Teaching Assistant for the course *"Numerical methods for differential equations"*, Department of Mathematics, University of Torino.

Teaching Assistant for the course *"Approximation methods"*, Department of Mathematics, University of Torino.

Teaching Assistant for the course *"Optimization methods"*, Department of Mathematics, University of Torino.

Lecturer for the project *"Diderot - Matetraining"*, CRT foundation, Torino.
This project was addressed to high school students, with the aim of divulging mathematics. I worked as teacher in 10 schools of Piemonte and Val d'Aosta involved into the project

Oral Communications

18-20 Feb 2014
EPIGEN 2014, *Progetto Bandiera Epigenomica (annual meeting)*, Roma, *Mathematical models on cancer progression*.

27-30 May 2014
Mathways into Cancer II , Carmona, *How steady states analysis helps cancer therapies*.

9 Jun 2011
CS2Bio, *International workshop on interactions between computer science and biology*, Reykjavik, *Mathematical approach to predict the drug effects on cancer stem cell models*.

Review Activity

International Conferences
- Petri Net 2013

International Journals
- Journal of Biomaterials and Nanobiotechnology

Attended Schools and Courses

16-28 Jul 2012
ICNDCS 2012, *Ph.D. School on Mathematical Modeling of Complex Systems (second edition)* , Pescara,
http://www.nodycosy.unich.it/index.php?phdsch2012.

1-2 Mar 2012
RNA-seq Workshop, *An introductory course to GeneChip Exon 1.0 ST NGS microRNA data analysis* , Torino,
http://www.bioinformatica.unito.it/exon.array.course.html.

27 Jun - 1 Jul 2011
CSAMA 2011, *Computational Statistics for Genome Biology (ninth edition)* , Bressanone,
http://marray.economia.unimi.it/2011/.

23-25 Feb 2011
Data Analysis Workshop, *An introductory course to RNA-seq* , Torino,
http://www.bioinformatica.unito.it/RNAseq.course.html.

REFERENCES

Prof. Gianfranco Balbo
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Prof. John Tyson
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Virginia Tech
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Dr. Francesca Cordero
Department of Computer Science
University of Torino
✉ fcordero@di.unito.it

PUBLICATIONS

International Journals

[J1] **C. Fornari**, G. Balbo, SM. Halawani, O. Ba-Rukab, AbR. Ahmad, RA. Calogero, F. Cordero and M. Beccuti. A versatile mathematical pipeline to explore how Cancer Stem Cell fate influences tumor progression. *BMC Bioinformatics [in revision]*, 2014.

[J2] **C. Fornari**, M. Beccuti, S. Lanzardo, L. Conti, G. Balbo, F. Cavallo, RA. Calogero, and F. Cordero. A mathematical-biological joint effort to investigate the tumor-initiating ability of cancer stem cells. *PLOS One*, 9, 2014.

[J3] M. Beccuti, **C. Fornari**, G. Franceschinis, SM. Halawani, O. Barukab, AB.R. Ahmad, and G. Balbo. From symmetric nets to differential equations exploiting model symmetries. *The Computer Journal*, 2013.

[J4] F. Cordero, M. Beccuti, **C. Fornari**, S. Lanzardo, L. Conti, F. Cavallo, G. Balbo, and RA. Calogero. Multi-level model for the investigation of oncoantigen-driven vaccination effect. *BMC Bioinformatics*, 14, 2013.

In Proceedings

[P1] F. Cordero, **C. Fornari**, M. Gribaudo and D. Manini. Markovian Agents Population Models to study Cancer Evolution. In *Proceedings of ASMTA '14: 21st International Conference on Analytical & Stochastic Modelling Techniques & Applications*, Budapest, Hungary, 2014. Springer Verlag Lecture Notes in Computer Science (LNCS) series.

[P2] **C. Fornari**, F. Cordero, D. Manini, RA. Calogero, and G. Balbo. Mathematical approach to predict the drug effects on cancer stem cell models. In *Proceedings of CS2Bio'11: 2nd International Workshop on Interactions between Computer Science and Biology*, Reykjavik, Iceland, 2011. ELSEVIER Electronic Notes in Theoretical Computer Science (ENTCS) series.

[P3] F. Cordero, **C. Fornari**, F. Cavallo, S. Lanzardo, L. Conti, D. Manini, M. Arigoni, G. Balbo, and RA. Calogero. Cancer stem cell based adjuvant for oncoantingen-driven vaccination. In *Proceedings of BCB' 11: ACM International Conference on Bioinformatics, Computational Biology and Biomedicine Proceedings*, Chicago, USA, 2011. ACM Digital Library.

Abstracts and Posters

[C1] **C. Fornari**, M. Beccuti, S. Lanzardo, L. Conti, F. Cavallo, G. Balbo, RA. Calogero, and F. Cordero. A mathematical perspective on cancer stem cell dynamics. In *Roma, BITS Annual Meeting*, 2014.

[C2] **C. Fornari**, F. Cordero, M. Beccuti RA. Calogero, and G. Balbo. Zoom-in and zoom-out on tumor progression. In *Udine, BITS Annual Meeting*, 2013.

[C3] **C. Fornari**, F. Cordero, M. Beccuti, RA. Calogero, and G. Balbo. How steady state analysis helps cancer therapies. In *Carmona, II workshop mathways into cancer*, 2013.

[C4] F. Cordero, **C. Fornari**, M. Beccuti RA. Calogero, and G. Balbo. The multi-level view to investigate the cancer progression. In *Carmona, II workshop mathways into cancer*, 2013.

[C5] **C. Fornari**, F. Cordero, M. Beccuti, S. Lanzardo, L. Conti, F. Cavallo, G. Balbo, and RA. Calogero. Multi-level model for the investigation of oncoantigen-driven vaccination effect. In *Barcelona, 16th RECOMB*, 2012.