Pre-clinical and clinical research

<table>
<thead>
<tr>
<th>Time</th>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:20</td>
<td>14:30</td>
<td>Sviluppo di algoritmi per la medicina personalizzata</td>
<td>Francesca Cordero</td>
</tr>
<tr>
<td>14:30</td>
<td>14:40</td>
<td>Modelli computazionali per lo studio di sistemi biologici</td>
<td>Marco Beccuti</td>
</tr>
<tr>
<td>14:40</td>
<td>14:50</td>
<td>Immagini digitali biomediche: simulazione ed elaborazione</td>
<td>Marco Grangetto/ Nello Balossino</td>
</tr>
<tr>
<td>14:50</td>
<td>15:00</td>
<td>HPC4AI: Centro servizi e calcolo per AI and edge computing</td>
<td>Marco Aldinucci e Giorgio Audrito</td>
</tr>
</tbody>
</table>
Sviluppo di algoritmi per la medicina personalizzata

Francesca Cordero
fcordero@di.unito.it
Deep sequencing technologies

Data Analysis - New insights: fusion genes

The molecular landscape of colorectal cancer cell lines unveils clinically actionable kinase targets.

M. Beccuti, et al., *Bioinformatics*, 2014

Prof. Alberto Bardelli
Prof. Enzo Medico

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione - Cordero Francesca
Clinical Biomarker discovery

Colorectal Cancer

Tumor cells show:
- Altered expression levels of several miRNAs
- Loss of tumour-suppressor miRNAs
- Accumulation of oncomiRNAs

Bladder Cancer

Ferrero G, et al., *Oncotarget*, 2018

Dr Alessio Naccarati
Dr Barbara Pardini
Dr Mario Trompetto
Dr Carlo Senore

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione - Cordero Francesca
Clinical Biomarker discovery - New frontiers: The Microbiome

10x more microbial than human cells

1M times as many microbes inside each of us than humans on earth

100x more microbial than human genes

Who is there?
What are they doing?
Clinical Biomarker discovery - New frontiers: The Microbiome

**Oncobiome:** the study of the interplay between the human microbiome and cancer development

---

Tarallo S, et al., *ISME*, 2018 - Under Review

---

Prof Nicola Segata
Cancer clones identification

Leukemia - Minimal Residual Disease Analysis
ImmunoGlobulin Heavy chain (IGH) rearrangement as molecular marker of clonality

An high level of ITH affects the high-grade serous epithelial ovarian cancer

Dr Mario Boccadoro
Dr Simone Ferrero

Beccuti M, et al., *BMC Bioinfo*, 2017

Prof. Flavia Di Renzo
UNIVERSITY OF TORINO
PhD Programme: Complexity in Life Sciences

Functional characterization of the Human noncoding genome by integrative analysis of High Throughput data

Giulio Ferrero
Laura Follia
Greta Romano
Giulia Piaggeschi
Raffaele Calogero

Niccolò Totis

Francesca Cordero

Gianfranco Balbo
Marco Beccuti
Susanna Donatelli

Simone Pernice

Biology Science
Medical Science
Mathematics
Computer Science

Collaborations
Pre-clinical and clinical research

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:20</td>
<td>Sviluppo di algoritmi per la medicina personalizzata</td>
<td>Francesca Cordero</td>
</tr>
<tr>
<td>14:30</td>
<td>Modelli computazionali per lo studio di sistemi biologici</td>
<td>Marco Beccuti</td>
</tr>
<tr>
<td>14:40</td>
<td>Immagini digitali biomediche: simulazione ed elaborazione</td>
<td>Marco Grangetto/ Nello Balossino</td>
</tr>
<tr>
<td>14:50</td>
<td>HPC4AI: Centro servizi e calcolo per AI and edge computing</td>
<td>Marco Aldinucci e Giorgio Audrito</td>
</tr>
</tbody>
</table>
Computational models to study biological systems

Marco Beccuti

beccuti@di.unito.it

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione
A biological system is a complex network of biologically relevant entities.

In Systems Biology mathematical and computational modeling can help scientists in the study of biological systems.
Computational models to study biological systems

- A biological system as a composition of sub-models with different time and space scales

- Sub-models can be parameterized using different input data.

**Challenge**

*How to efficiently model and study biological systems*
Computational models to study biological systems

- **Different modeling approaches** can be exploited according to the specific biological question and system.

### Interaction-based models
- Protein-protein interaction networks
- Gene regulatory networks
- Gene networks

### Constraint-based models
- Metabolic networks (in steady state)
- Flux balance analysis
- Optimization with linear programming

### Mechanism-Based models
- Metabolic networks
- Signal transduction pathways
- Cell population
- Epidemiological systems
- Differential equations
- Monte-Carlo simulation algorithms
- Dynamic behavior analysis

---

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione – **Marco Beccuti**
Computational models to study biological systems

◆ Our tools and methodologies:

A modeling framework based on **graphical formalism** which provides **different analysis techniques**

- **interaction-based approaches**
  - linear algebra;
  - CTL model checking.

- **constraint-based approaches**
  - Flux balance analysis;

- **mechanism-based approaches**
  - numerical techniques;
  - Ordinary Differential Equation (ODE) approximation;
  - Stochastic Differential Equation (SDE) approximation;
  - Monte-Carlo simulation.


**Computational models to study biological systems**

- **Application on breast ErbB2 cancer** in collaboration with Cavallo’s group (Dip. di Biotecnologie Molecolari e Scienze per la Salute – Univ. di Torino).

- **Goal:** to exploit the model to study different vaccination therapies of ErbB2 and TLR2.

- A 2-level model to study ErbB2 breast cancer progression:
  - ErbB2 is a transmembrane protein;
  - 20% of breast cancers overexpresses ErbB2;
  - ErbB2 is an appropriate target for therapies.

---

**F. Cordero, M. Beccuti, C. Fornari, S. Lanzardo, L. Conti, F. Cavallo, G. Balbo and R. Calogero.** Multi-level model for the investigation of oncoantigen-driven vaccination effect. International Journal BMC Bioinformatics, Volume 14, Suppl. 6, 2013

---

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione – Marco Beccuti
Computational models to study biological systems

• Application on cancer metabolism in collaboration with Novelli’s group (Dip. di Biotecnologie Molecolari e Scienze per la Salute – Univ. di Torino).

• Goal: To develop a new modeling approach to dealing with indetermination in biochemical networks.

We investigate the Warburg Effect in PDAC patients

Computational models to study biological systems

- **Application on Computational Epidemiology:** in collaboration Paolotti’s group (ISI foundation), Tozzi’s group (Area di ricerca Malattie Multifattoriali e Malattie Complesse - Ospedale Bambin Gesù) and Ghetti’s group (Adres srl).

- **Goal:** To develop a model to study the effects of different vaccine policies on pertussis epidemiology.

An extension of classical SIRS infection model was developed to include the peculiarities of the pertussis infection and the relative vaccination cycle.
Computational models to study biological systems
# Pre-clinical and clinical research

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:20</td>
<td>Sviluppo di algoritmi per la medicina personalizzata</td>
<td>Francesca Cordero</td>
</tr>
<tr>
<td>14:30</td>
<td>Modelli computazionali per lo studio di sistemi biologici</td>
<td>Marco Beccuti</td>
</tr>
<tr>
<td>14:40</td>
<td>Immagini digitali biomediche: simulazione ed elaborazione</td>
<td>Marco Grangetto/ Nello Balossino</td>
</tr>
<tr>
<td>14:50</td>
<td>HPC4AI: Centro servizi e calcolo per AI and edge computing</td>
<td>Marco Aldinucci e Giorgio Audrito</td>
</tr>
</tbody>
</table>
Digital image processing @ di.unito.it

• **Who?** [http://di.unito.it/EidosLab](http://di.unito.it/EidosLab) founded in 1985

• **What?**

Biomedical Image processing

Simulations and virtual reality

Medical data integrity

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell’Innovazione – *Marco Grangetto, Nello Balossino*
Biomedical image processing

• Usage of standard tools and design of novel methods for
  • Detection
  • Segmentation
  • Classification
  • Tracking
  • Enhancement

• Applications areas:
  • Clinical diagnosis support
  • Preclinical research
Recent & ongoing activities

- Automatic microtubule tracking in fluorescence images
- Eidos+MBC+POLITO


Recent & ongoing activities

• Tumor segmentation from dynamic PET acquisitions
• Eidos + IRCCS Candiolo (Medical Physics department)


Recent & ongoing activities

• Deep learning for histopathological characterization of colorectal polyps (Eidos+ prof. Paola Cassoni)

• Estimation of Ph maps from MRI images (Eidos + prof. Dario Longo)
Future works

• Since 2012 DeepLearning is fostering a lot of interests in the area of automatic image interpretation: tremendous potential impact on imaging based diagnosis (needs of interdisciplinary research + large and well engineered datasets)

**DeepHealth**: Deep-Learning and HPC to Boost Biomedical Applications for Health


• Involves 21 partners (Spain, Italy, Netherlands, Germany, Sweden, Switzerland, Romania, Greece) including Unito e Città della Salute

*The main goal of the DeepHealth project is to put HPC computing power at the service of biomedical applications with DL needs and, through an interdisciplinary approach, apply DL techniques on large and complex biomedical datasets to support diagnosis and to generate insights into complex diseases in a scalable and efficient way.*
DeepHealth at a glance
Medical image integrity

• Verification of medical image integrity by using invisible and reversible watermarking (content validation, secure diagnosis and metadata handling)

Eidos + AOU Città della Salute + ASL CN2 Alba Bra

Brevetto italiano nr. 0001419815: Procedimento e sistema per marcare immagini mediche tramite una tecnica di "watermarking" fragile e reversibile utilizzando un metodo statistico e firma digitale


Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione – Marco Grangetto, Nello Balossino
Virtual training for radiologist

- Simulation of the RX image acquisition for training in collaboration with Città della Salute

**Real scenario**

**The simulation**

1. Virtual radiological room
2. Radiography preview
3. Image histogram

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell’Innovazione – Marco Grangetto, Nello Balossino


<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:20</td>
<td><strong>Sviluppo di algoritmi per la medicina personalizzata</strong></td>
<td>Francesca Cordero</td>
</tr>
<tr>
<td>14:30</td>
<td><strong>Modelli computazionali per lo studio di sistemi biologici</strong></td>
<td>Marco Beccuti</td>
</tr>
<tr>
<td>14:40</td>
<td><strong>Immagini digitali biomediche: simulazione ed elaborazione</strong></td>
<td>Marco Grangetto/ Nello Balossino</td>
</tr>
<tr>
<td>14:50</td>
<td><strong>HPC4AI: Centro servizi e calcolo per AI and edge computing</strong></td>
<td>Marco Aldinucci e Giorgio Audrito</td>
</tr>
</tbody>
</table>
The Turin’s centre on High-Performance Computing for Artificial Intelligence

Prof. Marco Aldinucci

Computer Science Department, University of Torino
HPC4AI: AI-on-demand platform

Regione Piemonte INFRA-P call Nov. 2017 - 4.5M€ total cost - Coord. M. Aldinucci
2 funded partners - 8 associated partners - Many industrial stakeholders
Turin’s HPC4AI centre
A one-stop-shop for AI and BDA

- **Data** - to store data & datasets
  - Securely, preserving ownership, always available

- **Processes** - to develop new protocols
  - Cross-pollinating computer and life sciences
  - Automation and continuous improvement of processes

- **Performance** - to ease the access to HPC
  - For Machine Learning and BigData on-demand
Data: Storage for life science research

- Large, highly accessible, robust space
  - >5PB of space with 20Gb/s PoP on GARR backbone
  - Backup, encryption (on-demand)

- Federated cloud access
  - Preserving ownership and full control on accesses
  - Ease sharing on-demand (by way of the federation)

- Compute available on-site
  - Move TB for each data analysis is not really handy

- A marketplace of high-quality datasets
  - E.g. UNESCO software heritage
  - E.g. as imagined in ICT11a “Deepheath” with Cassoni (pathology) & Bergui (radiology)
Processes: Automatise existing processes and protocols and improve them
Processes: Automatise existing processes and protocols and improve them.

PaaS
Processes: Automatise existing processes and protocols and improve them

IaaS
<table>
<thead>
<tr>
<th>Users</th>
<th>Kind of service</th>
<th>Services</th>
<th>Artifacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domain experts with no skills on ML and BDA.</td>
<td>Service-as-a-Service (SaaS)</td>
<td>SaaS for ML and BDA designed within HPC4AI partners</td>
<td>Market place for ML and BDA services: Dashboards, trained models in several domains (NLP, Vision, …)</td>
</tr>
<tr>
<td>Domain experts skilled on ML and BDA. Not expert in parallel computing.</td>
<td>Platform-as-a-Service (PaaS)</td>
<td>PaaS solutions for ML and BDA directly designed within HPC4AI or companion projects</td>
<td>Market place of VMs and Platforms realising software stacks for ML and BDA. Solutions for data ingestion, data lake, etc.</td>
</tr>
<tr>
<td>Researchers, cloud engineering, ML and BDA framework designers, cloud engineers, stack and automation designers.</td>
<td>Infrastructure-as-a-Service (IaaS)</td>
<td>GARR/other cloud able to support federation</td>
<td>Openstack, docker, VM, object storage, file storage, kubernetes, etc.</td>
</tr>
<tr>
<td>Researchers, run-time designers.</td>
<td>Hardware</td>
<td>Bare Metal</td>
<td>Multicore, GPU, storage, network, switch, UPS, cooling, etc.</td>
</tr>
</tbody>
</table>
Compute: VMs, HPC queues and much more

- 5000+ cores, 40+ GPUs (200K cuda cores), 1TB RAM per node (on some nodes), …
Imagine next generation data management for life science

1. Start from existing data
   - Store, share, sell: under the full control of owner

2. Imagine AI support
   - For scoring, support and automation - not for diagnosis

3. Evaluate annotation, improve the process
   - Imagine how to improve protocols/processes and annotation to be better automatised and AI-supported

4. Develop novel analysis techniques and GOTO 3
   - Continuous improving of processes by cross-pollinating computer and life science
## Pre-clinical and clinical research

<table>
<thead>
<tr>
<th>Time</th>
<th>Time</th>
<th>Topic</th>
<th>Presenter/Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:20</td>
<td>14:30</td>
<td>Sviluppo di algoritmi per la medicina personalizzata</td>
<td>Francesca Cordero</td>
</tr>
<tr>
<td>14:30</td>
<td>14:40</td>
<td>Modelli computazionali per lo studio di sistemi biologici</td>
<td>Marco Beccuti</td>
</tr>
<tr>
<td>14:40</td>
<td>14:50</td>
<td>Immagini digitali biomediche: simulazione ed elaborazione</td>
<td>Marco Grangetto/ Nello Balossino</td>
</tr>
<tr>
<td>14:50</td>
<td>15:00</td>
<td>HPC4AI: Centro servizi e calcolo per AI and edge computing</td>
<td>Marco Aldinucci e Giorgio Audrito</td>
</tr>
</tbody>
</table>
**Aggregate Computing @ di.unito.it**

**Who?** System Modelling, Verification and Reuse ([http://di.unito.it/movere](http://di.unito.it/movere))

**Why?** In the context of Working Group 4 (Application areas outside “pure” software reliability) of the EU COST Action IC1402 ARVI (Runtime Verification beyond Monitoring, [https://www.cost-arvi.eu](https://www.cost-arvi.eu))

**What?** Edge computing technology for monitoring:
- medical devices
- hospital wards
- operating rooms
- laboratories
- ...

---

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione - **Audrito Giorgio**
Elastic Cloud Backend

Storage Elaboration and statistics

Real Time Elaboration and DSS

Fog/Edge Node

Data

Patient Health Record

Laboratory Instruments

Real time Monitoring

Portable Devices

Cloud Middleware

Fog/Edge Middleware

IoT Middleware

Model

Toolchain

Methodology

Aggregate processes

Dipartimento Informatica nel Parco della Salute, della Ricerca e dell'Innovazione - Audrito Giorgio