



e-Science for Cancer
Prevention and Control

**Individualised cancer prevention and eCPC
– can e-Science tools be used to save lives and reduce costs?**

pages 3–4

SeRC firmly in place

This is the second SeRC newsletter and we have now roughly reached the half time in the first five years of SeRC. The SeRC organization and the activities we will concentrate on during the first phase are now firmly in place and most of the funding has been allocated. It is with great pride that I look at all the progress we have had so far, and it also gives me confidence that we are in a good position to achieve an excellent evaluation after the first five years. Should we get a positive evaluation, the funding will become permanent and SeRC will survive for many years to come.

During the last year, the third annual meeting of SeRC took place on April 24–25, at the lovely surroundings of Skogshem & Wijk in Lidingö. About 110 participants attended the conference. Several prominent speakers were invited, including William T.C. Kramer (NCSA, University of Illinois) who talked about the challenges of petascale computing and David Jones (University College London) who discussed e-Science in the context of bioinformatics. Mathias Uhlén, Managing Director of SciLifeLab and the new Director of SNIC, Jacko Koster, were also giving talks. Marcus Nordenstam from Exotic Matter, who described and showed examples of computational fluid dynamics applications in Hollywood movies, ended the first day of presentations. In the evening there was a well-visited poster session and a “core-community drop-in”, where representatives from the core communities had an open house for the rest of the participants.

Another important activity during the last year was the formation of the SeRC Faculty. The SeRC faculty consists of all community coordinators and senior researchers with substantial funding from SeRC. Both core and applied areas are represented, as well as all four universities. The main goal of the faculty is to facilitate interdisciplinary exchange between applied and core e-Science communities, and to provide SeRC with an inter-community-network of e-Science researchers. The faculty also has a voice in the steering of SeRC, advising the director and management board on scientific issues. The members of the faculty constitute the main driving force of research projects within SeRC, e.g. as supervisors or co-supervisors of PhD projects. The faculty organizes scientific workshops on specific e-Science related questions and constitutes a forum for joint applications. It is also responsible for integrating application experts within the communities. The faculty has two larger meetings each year, in between which there are smaller workshops and community-meetings. Together with the application experts the faculty plays an important role as the scientific “engine” of SeRC, realizing the vision from our strategy: “Through e-Science enable world leading research within strategically important areas”.

In this issue of the newsletter you can read more about our new flagship project, the advisory board, SeRC faculty and community activities, and the latest faculty meeting we organized together with the application experts (AE) at PDC and NSC. The recent meeting between the SeRC Faculty and the application experts was a great success and will surely facilitate the important mission of the application experts to be the glue between the core and the applied communities. New community coordinators are also presented in this issue.



DAN HENNINGSON
SeRC DIRECTOR

New Community Coordinators

SeRC management have had an ambition to involve the SeRC faculty more into the management of the communities, and during the last year several new Community Coordinators have been appointed, such as Björn Wallner for the Bioinformatics Community, Rodrigo Caballero for the Climate Community, Timo Ropinski for the Visualization Community, Tino Ebbers for the Medical Visualization Subcommunity, Jeanette Hellgren-Kotaleski for Complex Diseases and Lars Bergqvist for Electronic Structure.



Björn Wallner
Bioinformatics Community
Coordinator



Rodrigo Caballero
Climate Community
Coordinator



Timo Ropinski
Visualization Community
Coordinator



Tino Ebbers
Medical Visualization
Subcommunity Coordinator



Jeanette Hellgren-Kotaleski
Complex Diseases
Community Coordinator



Lars Bergqvist
Electronic Structure
Community Coordinator



Participants at the third annual meeting of SeRC, April 24–25, 2012, Skogshem & Wijk, Lidingö

e-Science for Cancer Prevention and Control (eCPC) – a flagship project at the Swedish e-Science Research

Why do some people get cancer while others do not? Why do some people die of their cancer while others do not? Could more targeted screening and prevention programmes save lives? Can improved data integration and more sophisticated modelling and simulation tools make a difference?

The SeRC flagship project e-Science for Cancer Prevention and Control (eCPC) will set up a modular system for prediction of cancer initiation and progression. It will be based on computational models that integrate data from different sources, including molecular (e.g. genomic, proteomic), environmental and life-style factors. By superimposing screening and prevention strategies on the models, reduced over-treatment, morbidity, mortality and cost can be quantified.

eCPC works in close collaboration with two research centres: (i) The “Cancer Risk Prediction Center” (CRiSP), a Swedish Research Council-funded Linneaus Centre focused on prevention of breast and prostate cancer, and (ii) the project “Advancing Cervical Cancer Eradication Strategies (ACCES)”, funded by the Clinical Research Programme of the Swedish Foundation for Strategic Research.

The eCPC provides e-Science tools for planning, evaluating and adapting individualized screening and prevention programmes. This constitutes a refinement over the current ‘one screening strategy fits all’ for breast mammography screening and for cytology-based cervical cancer screening and it augments the widespread opportunistic PSA testing for prostate cancer.



Participants in the eCPC kickoff meeting at Sandhamn, May 9–10 2012. The meeting featured presentations from all work package leaders as well as invited speakers.

Two-fold objectives

The large and complex system of data integration, modelling and simulation in eCPC requires multi-disciplinary expertise and aims at building generic tools for translational research.

The broad objectives of eCPC are two-fold:

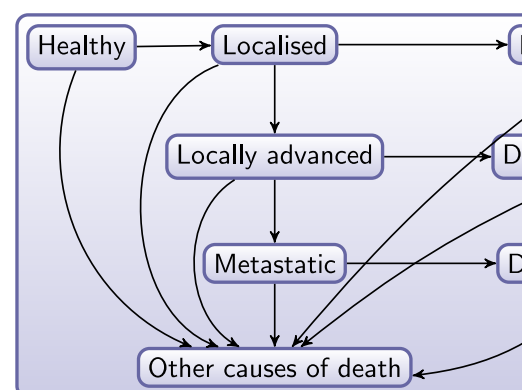
“Assess how novel prevention and screening strategies superimposed on the models for cancer initiation, detection and progression can simultaneously avoid over-treatment and reduce death from cancer” and

“Investigate how the modular eCPC data integration, modelling and simulation framework can be used as a generic template for other research questions on screening and prevention and in other disease domains.”

Work Plan

At the heart of eCPC is the micro-simulation engine, which relies on integrated data from many sources, including population and health registries, biobanks, biotechnology platforms and data from research projects.

The initial applications are for cancers of the cervix, prostate and breast. Using individual-based markers together with traditional screening measures are expected to improve specificity (reduce rate of false positives) without jeopardizing sensitivity (ability to detect tumours). Since the system against which to evaluate screening strategies is too complex to be captured by a single analytic probabilistic model, a large number of individual



A simplified natural history sub-model for prostate cancer, cancer (second column) to detected cancer (third cancer) for PSA testing, clinical diagnosis and prostate cancer treatment screening intervals and treatment strategies on a simulated

life histories in a population and a large number of such populations are simulated in silico. The structure and the parameters of the life histories are derived from in-house and published sources and will be updated and refined as more knowledge accumulates. Model output is measured as reduced over-treatment, morbidity, mortality and cost. Calibration methods will be developed to assess model fit.

eCPC is divided into five work-packages (WPs), and special emphasis is put on developing:

- A micro-simulation engine based on solid software engineering and code optimization (WP1 and WP3).
- Generic tools for data integration and exchange. These include data availability systems for querying the content of data sources as well as secure ways for electronic transport and merging of anonymised data (WP1 and WP2).
- Probability models, systems biology algorithms, prediction tools and calibration methods as the structural basis for the micro-simulation modules (WP3, WP4 and WP5).

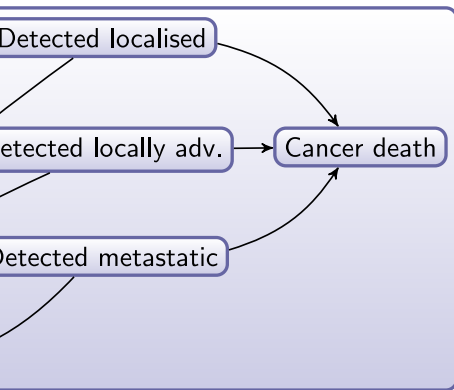
The five work-packages of eCPC and the work-package leaders are listed below:

WP1: Data integration, software engineering and code optimization
(Ola Spjuth, Karolinska Institutet (KI))

WP2: Data security
(Jim Dowling, SICS/KTH)

WP3: Micro-simulation
(Mark Clements, KI)

Health Centre (SeRC)



describing the pathway from healthy to latent to death. This pathway is overlaid with sub-models of treatment, and allows for evaluating hypotheses such as the effect of population.

WP4: Systems biology algorithms
(Sampsa Hautaniemi, University of Helsinki)

WP5: Prediction and screening models
(Keith Humphreys, KI)

eCPC Organization

eCPC PIs: Juni Palmgren (SeRC Complex Diseases e-Science Community) and Jan-Eric Litton (SeRC Data Management Core Community)

Steering group: Jan-Eric Litton, Juni Palmgren, Pär Sparen, Ola Spjuth, Mark Clements, Martin Eklund, and Keith Humphreys

Management group: Ola Spjuth, Juni Palmgren, and Mark Clements

Project leader: Ola Spjuth

Project co-leader: Mark Clements

A scientific advisory board is currently being established.

Project website:

www.e-science.se/community/eCPC



eCPC PI: Juni Palmgren and Jan-Eric Litton
Department of Medical Epidemiology and Biostatistics,
Karolinska Institutet

Interview with Ola Spjuth, project leader of eCPC and WP1



Could you explain the motivation behind the data integration part of eCPC?

Sweden has extraordinarily good resources for research in the life sciences with extensive data on patients and samples stored in various registries and biobanks. The microsimulation (WP3) relies extensively on data from hospitals and research datasets. However, today it is problematic to get an integrated view of the available sources, and eCPC aims at developing technical solutions for this.

Who are the users and what will be the benefits to them?

eCPC will provide scientists and other users with the possibility to query all relevant data sources through a simple user interface and experiment with parameters, investigating e.g. the size of an integrated dataset that could be assembled if data from different sources were collected and combined.

Could you explain how you deal with sensitive data?

In the short term we will focus on tools for data availability, which means that no actual raw data values are integrated through this platform but only the notion that data about a certain sample or patient exist in e.g. a biobank or registry. We also use anonymisation techniques to ensure that the risk of re-identification is low enough. Also, we aim at improving security using other technologies, such as Yubikey.

Interview with Alex Ploner, working on cervix cancer in WP3 and WP5



What is the background to the project?

Cervical cancer is a rare success story among cancers: screening has reduced the number of cancer cases by 2/3 since the 1960s. We know now that the human papillomavirus (HPV) is a necessary cause for developing cervical cancer and we have vaccines that can prevent 70% of these infections. The challenge for public health is how to combine the two: what kind of cervical screening will maximize benefits for a mixture of vaccinated and unvaccinated women?

How will microsimulation help you answer those research questions?

There is no way to implement an evaluation trial quickly, so we're using microsimulation to evaluate a wide range of options.

What is new?

We are using an existing natural history model in several innovative ways: first, as part of the ACCES project, we will use a huge national database on cancer and screening to make the model more valid in our setting. Second, Alexandra Jauhiainen, a postdoc in eCPC, is adapting state-of-the-art methods for model fitting and calibration. Finally, computationally, we are tied into the national infrastructure, with access to hardware and software expertise, so we should be able to efficiently run more complex models for a wider range of options.

What are you currently working on?

Most of the mathematics has been put on paper, so we are now focusing on the implementation: we want something that runs out of the box, which is easily adaptable and computationally efficient. So we're working on abstracting the biological and technical details into one layer, and the calculation engine into another layer. And we'll use open source software throughout, implementing the top layer in R [an open-source statistical environment], and we'll use R to distribute the code under the GPL [GNU Public Licence, a popular open source licence], so we have full transparency and allow anyone to work with our model."

SeRC faculty and community activities during 2012

The first meeting of the SeRC faculty took place at Villa Brevik Mars, 22–23, 2012. The objective of the meeting was to learn to know each other better and to get a common view of the role and goals of the SeRC faculty. In line with one of the goals conceived at the meeting, i.e. to facilitate interdisciplinary exchange between core and applied e-Science research, a number of inter-community workshops took place after the faculty meeting.

These workshops include “Electrostatics in Molecular Simulations”, March 16, in collaboration between the Numerical Analysis and the Molecular Simulations Community, “e-Science for Cancer Prevention and Cure”, May 9–10, in collaboration between the Complex Diseases and Data Management communities, a “SeRC Visualization Workshop”, May 21, with the aim to “bring together domain experts and core researchers to address visualization challenges in e-Science”, at the Norrköping Visualization Center C.

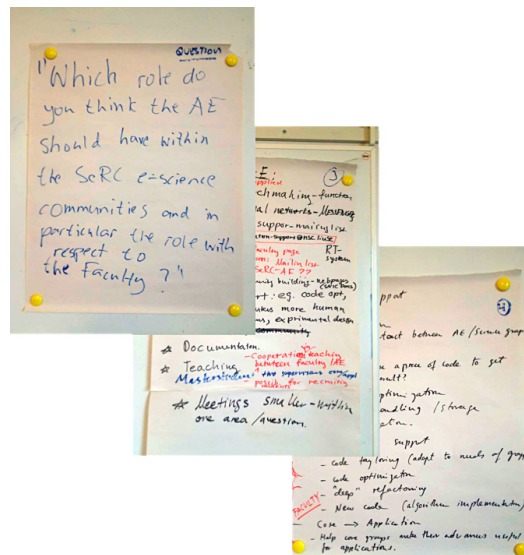
There was also the SeRC Bioinformatics workshop Feb 1–2.

Apart from the workshops there has been a seminar series in Molecular Dynamics during the spring, a “core-community drop in” at the SeRC annual meeting, April 24, a SeRC seminar with Professor Paul F. Fischer Sep 3 with more than 100 participants, and a summer school on Numerical Methods for Multiphase Flows, Sep 3–7.

A second faculty meeting took place October 19 at the Rica hotel in Stockholm. This time the SeRC application experts were invited and the theme of the meeting was “Integration of the application experts into the e-Science communities”. One conclusion from the meeting was that both faculty as well as application experts wanted more long-term projects for the application experts, and that the faculty needs to take an active role in defining the projects the application experts work with. Several concrete

suggestions for integrating the application experts into the e-Science communities came up including mailing lists, community-application expert meetings, and an application expert-open-house at the next annual meeting.

OLIVIA ERIKSSON



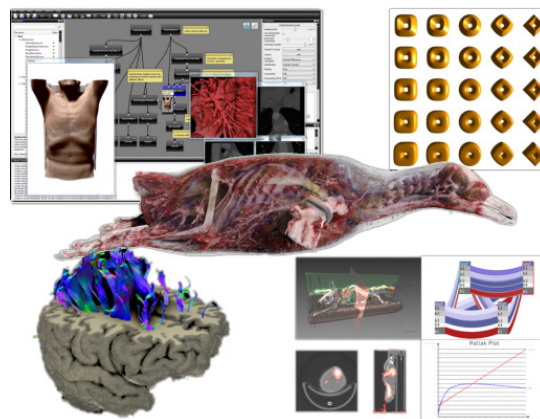
New collaborations within Visualization

Within the visualization community, several new projects have been launched since the visualization workshop, which took place in May 2012 in Norrköping. The collaboration between Scientific Visualization, Norrköping and Material Science, Linköping was further strengthened. Peter Steneteg, a new PostDoc with a background in material science, will spend part of his working time in the Visualization Center C, and cooperate with the newly hired research engineer Sathish Kottraval. The goal is to cooperatively

improve the understanding of complex grid structures through visualization.

Furthermore, Sathish focuses on large data support which is the basis for cooperations with the FLOW and the Climate Modeling community. Besides this effort, projects are also conducted within the Medical Visualization subcommunity. Recent progresses tackle 4D blood flow in MRI data as well as the visualization of multivariate medical data.

TIMO ROPINSKI

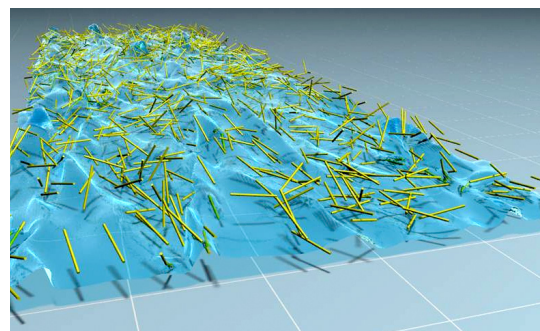


Simulations of turbulent Fibre Suspension

A mathematical model of a turbulent fibre suspension flowing through a channel was applied to study the dynamical behavior of finite-size rigid fibres. The model specifically applies to the flow of pulp suspensions through a papermachine headbox. The turbulent flow was modeled by an entropy lattice Boltzmann method and the interaction between fibres and carrier fluid was modeled through an external boundary force method.

Direct contact and lubrication force models for fibre-fibre interactions and fibre-wall interaction were taken into account to allow for a full four-way interaction. Unlike earlier findings for point-like fibres or small spherical particles, the finite size of the fibre had a clear influence on the dynamics of the suspension. Specially, at the region close to the wall.

MINH DO-QUANG



Murder Mystery Mummy

One of the key attractions in the Early Egypt gallery (Gallery 64) at the British Museum is the body of a man who was buried in about 3500 BC at the site of Gebelein in Upper Egypt. Direct contact with the hot dry sand naturally dried and mummified his remains.

At the Visualization Center – C in Norrköping, hosting the SeRC research efforts on Visualization, fundamental work on volumetric rendering and shading has led to the development of a virtual autopsy table on which a scan of the mummy

is now shown. Using the interactive touchscreen, it is possible to strip away the skin to expose the skeleton, and make virtual slices to view internal organs and the brain. Using the table scientist at the British Museum also discovered that the Gebelein most likely was murdered. The cause of death was established with the help of forensic radiologist Anders Persson at CMIV in Linköping. The table is currently being trialed in Gallery 64 and lets visitors to the British Museum explore this natural mummy for themselves.

ANDERS YNNERMAN



SeRC Advisory group



Morten Dæhlen, Professor,
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Björn Engquist, Professor,
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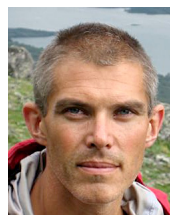
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Mattias Sillén, PhD,
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The Advisory group of SeRC consists of participants from academia as well as industry and meets once a year together with the SeRC Steering group. They discuss and comment upon the results and strategy of SeRC, and this is summarized in a yearly report of recommendations.

Advice to SeRC

In the latest report the Advisory group was generally impressed by the amount of activities and the coordination obtained within SeRC, and expressed that SeRC has had a very promising start both at management level and within the selected projects conducted by the different communities.

The Advisory board gave some advice to SeRC, including the following:

- Prioritize the core communities, e.g. put extra effort into challenges with respect to data management and construction of information infrastructures.
- Select a flagship-project that strengthens the collaboration between applied and core communities.
- It should not be the goal of SeRC to cover as many research fields as possible outside the existing communities.
- Strengthen the collaboration between core and applied communities.
- Invest so that SeRC researchers improve their position with respect to funding from other resources.

- Secure the visibility of SeRC.
- Define a few metrics measuring the outcome of SeRC activities.
- Find efficient mechanisms involving the Application Experts into the various projects.

OLIVIA ERIKSSON

**Fourth Annual Meeting
of SeRC**

The fourth annual meeting
of SeRC will take place the
24th – 25th of April 2013 at the
Visualization Center – C, Norrköping.

