

Newsletter Issue No. 9 February 2020

Welcome

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I would like to welcome you to the first Newsletter of 2020 and of Comp-BioMed2, which started in October

2019 and will run for a further 4 years. As you will see in this newsletter, we have already had our Kickoff meeting and are busy enacting some of the plans that we determined during this meeting. We have two new partners in CompBioMed2, Leibniz Rechenzentrum (LRZ) in Munich, where we held our meeting, and the University of Bologna where we

welcome back Prof Viceconti and his new team to the Centre of Excellence.

In addition to the exciting research activities of the Centre, we also have various education, training and dissemination activities that are ongoing and are highlighted in this edition of the newsletter. We were pleased that F1000 research joined us as an Associate Partner near the end of CompBioMed1 and we are now able to highlight some of their work and we look forward to collaborating further with them.

Training opportunities are expanding too, with the *In Silico* World International School in Bologna. We are also laying out our funded Visitor Programme and encourage people to apply to this and expand their own and collaborator's research.

We are also very excited to announce that we have now run a benchmark on the full production partition of SuperMUC-NG supercomputer at LRZ. This work, using HemeLB, was looking at the blood flow in the whole human vasculature and brings us one step closer to modelling the whole human and to running on exascale machines of the future.

Finally we take a look at some of the events that CompBioMed is hosting and taking part in during the early part of the year, including a meeting centred around the use of high performance data analytics in which we will push forward the work that is already underway on data management, machine learning and artificial intelligence. We also discuss the final review meeting that took place at the Commission in November 2019 at which we were able to show the progress that we have made on the research, training and dissemination activities throughout the Centre of Excellence. It was encouraging for the future of the Centre and for the coming 4 years.

CompBioMed2 - Kick-off meeting

CompBioMed2 Kicks off at LRZ in Garching, Munich

In our Centre of Excellence we have established ourself as a hub for practitioners in the field of Computational Biomedicine, successfully nucleating a substantial body of research, education, training, innovation and outreach within this nascent field. Medical regulatory authorities are currently embracing the prospect of using *in silico* methods in the area of clinical trials. We intend to be in the vanguard of this activitiy, laying the ground-



work for the application of HPC-based computational biomedicine approaches to a greater number of therapeutic areas.

The HPC requirements of our users are as diverse as the communities we represent. We support all forms of computing patterns from monolithic, potentially scaling to the exascale, to complex workflows requiring rigorous uncertainty quantification and the embrace of the convergence of HPC and high performance data analytics (HPDA). The CompBioMed Centre of Excellence seeks to combine these approaches with the large, heterogeneous datasets from medical and clinical records, and from experimental laboratories to underpin clinical decision support systems.

As we move into the second phase of our Centre of Excellence we will continue to support, nurture and grow our community of practitioners, delivering incubator activities to prepare our most mature applications for wider usage, providing avenues that will sustain the Centre of Excellence well beyond the current funding period. To this end we have established new work packages in CompBioMed dedicated to Data Analytics and Incubator Applications.

Recent Publications

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- M. Viceconti, F. Pappalardo, B. Rodriguez, M. Horner, J. Bischoff, F. Musuamba Tshinanu, In silico trials: Verification, validation and uncertainty quantification of predictive models used in the regulatory evaluation of biomedical products, *Methods* (2020), DOI:10.1016/j.y.meth.2020.01.011
- F. Levrero-Florencio, F. Margara, E. Zacur, A. Beuno-Orovio, Z. J. Wang, A. Santiago, J. Aguado-Sierra, G. Houzeaux, V. Grau, D. Kay, M. Vazquez, R. Ruiz-Baier, B. Rodriguez, Sensitivity analysis of a strongly-coupled human-based electromechanical cardiac model: Effect fof mechanical parameters on phsiologically relevant biomarkers, *Comput. Methods Appl. Mech. Engrg.* (2020),

DOI: 10.1016/j.cma.2019.112762

- J. Tomek, A. Beuno-Orovio, E. Passini, X. Zhou, A. Minchole, O. Britton, C. Bartlucci, S. Severi, A. Shrier, L. Virag, A. Varro, B. Rodriguez, Development, calibration and validation of a novel human ventricular myocyte model in health, disease and drug block, *eLife* (2019), DOI: 10.7554/eLife.48890
- A. Alowayyed, M. Vassaux, B. Czaja, P.V. Coveney, A. G. Hoekstra, Towards Heterogeneous Multi-scale Computing on Large Scale Parallel Supercomputers, *Supercomputing Frontiers and Innovations*, (2019), DOI: 10.14529/jsfi190402

Toward the first full scale virtual human simulation at the exascale.

A major effort is now underway to perform the first full scale 3D high fidelity simulations of blood flow in the human vasculature. Led by Peter Coveney within his Centre for Computational Science (CCS) at University College London (UCL), this major, large scale interdisciplinary collaboration, involves colleagues and collaborators from across Europe and the USA. The members of the team include UCL, Leibniz Supercomputing Centre (LRZ), Jülich Supercomputing Centre (JSC), the IT'IS Foundation and the University of Tennessee at Chattanooga. LRZ, a core partner in our CoE, is providing the use of their new supercomputer, SuperMUC-NG, through a large scale, Gauss Centre for Supercomputing, award for 2019-20 with Prof Dieter Kranzlmüller and Prof Peter Coveney. JSC is involved via our sister CoE POP (https://pop-coe.eu) and has been working with us to optimise the performance of the HemeLB code, with Dr Brian Wylie at JSC. The IT'IS Foundation (https://itis.swiss/itis-for-health/), based in Zürich, Switzerland, is an associate partner of our CoE and has provided the vascular model data. Dr Jon McCullough is performing the scientific studies within the CCS at UCL which currently address the coupling of arterial and venous trees.

HemeLB is a massively parallel, highly scalable blood flow simulator optimised for sparse geometries such as those that are found in the human vasculature. Cur-



rently, it is a plain MPI code which scales impressively on all muticore platforms. With the advent of SuperMUC-NG, #9 in the Top500 list with almost 27 petaflops performance and over 300k cores, HemeLB has been ported to the behemoth and, after reporting very good benchmarks last November over one half of the machine, we were able to get access to the entire production partition in early February.

Using a scaling baseline with 18 compute nodes, the smallest possible run with the memory available on SuperMUC-NG, we find a 190x speedup (on 358,000 cores), which can be seen in the scaling plots of the work. The version of HemeLB, and associated patches, used for this work in addition to the dataset for the scaling runs, was provided by Dr Alex Patronis, who worked with Coveney at CCS before taking up a new position at JSC in mid



2019. Essential support was provided from LRZ to enable this opportunity to undertake large runs on SuperMUC-NG and we are grateful for their assistance in this work.

The performance of HemeLB seen in this work on SuperMUC-NG, one of the most powerful machines in the EU, is a very encouraging milestone on the path to the exascale. We are expecting the first exascale machines to be ready in the USA as early as 2021 and in the EU by 2023. With these and other machines we aim to run the first full scale virtual human simulations and expect such studies to become commonplace at and beyond the exascale.

Peter Coveney likens the endeavour to an assault on Mount Everest (or the North Face of the Eiger if you prefer): we've now left base camp and are moving toward Camp 2 ...

International School on *in silico* **Trials**

From 7-9 September 2020, University of Bologna and InSilico World will be hosting a 3-day International School on *in silico* trials. Until 2016 the development and validation of computer models to predict the progression of a disease, or the changes to such progression due to a specific treatment, were only of academic interest. This is because until then, for the purpose of regulatory approval, an evidence of safety or efficacy of a new medical product was acceptable only if it had been obtained experimentally, either *in vitro* (e.g. with tests on cell cultures), or *in vivo* (with animal experimentation or with clinical trials on humans).

But in the last three years the two main regulatory agencies, the US Food and Drugs Administration (FDA) and the European Medical Agency (EMA) have, in principle, deemed admissible a third way to produce such evidence: through *in silico* simulations, i.e. using computer models. The goal of this international school is to provide to all stakeholders within this realm an executive perspective on *in silico* trials through a three-day intensive school taught by some of the top specialists in the world.

The structure of the school is being organised as a SWOT (Strength, Weakness, Opportunity and Threat) analysis. After an introduction from the Chair of the International School, Prof Viceconti, four experts will evaluate the strengths and weaknesses of the four most popular classes of modelling methods, followed by a reflection on how high-performance computing can change. Then, six specialists will provide an overview of the opportunities that *in silcio* trials technologies offer in some of the most important classes of disease. Last, the threats posed by the complex regulatory landscape will be balanced in a vision of the possible futures of biomedical industry in the age of *in silico* trials.

To register for this event, visit: http://bit.ly/iswschool

CompBioMed Centre of Excellence Visitor Programme

So far within the CompBioMed CoE we have encouraged scientists within academia and industry to participate in a Visitor Programme in which a specific programme of work can take place in the field of computational biomedicine. The key driver of our network building activities in CompBioMed2 will be the provision of training to the computational biomedicine community on HPC access, usage and related software development, which is now complemented by a substantially funded Visitor Programme, which will encourage exchange of personnel between interested participants.

The Visitor Programme is a flexible scheme designed



to support knowledge exchange between two or more organisiations. at least one of which should be a Core or As-

sociate Partner but can involve a third party. Personnel at all levels will be able to draw on funds for conducting work to promote knowledge exchange in one or more partners of their choice.

Potential visitors should contact their preferred host institution(s) to ensure that the work is suitable and they are eligible to participate. Then the visitor should apply throught the online form at: https://www.compbiomed. eu/innovation/visitor-programme/. The visits can be of any duration betweeen one week and three months, up to a maximum of €5,000. Applicants will need to provide a detailed proposal including:

- A full description of the work (one to three pages)
- An estimate of the anticipated HPC requirements and how they would be used
- Justification of the chosen host institute •
- A proposal of the costs involved. •

The proposal can be written directly into the online form or as a Word or PDF document. Following the application, the proposal will be reviewed by the selection committee, subject to the following criteria:

- Alignment of the proposal with the strategic goals of CompBioMed judged against the Key Performance Indicators (KPIs) for the project
- Quality of the project proposal
- Potential impact of the project again in relation to the KPIs

Funds for the Visitor Programme, held at CBK Sci Con Ltd, will be reimbursed by them and therefore should be cleared with the company before the exchange takes place.

We anticipate that this additional support in the programme will encoourage further collaboration between Core and Associate Partners and will incorporate researchers and industry from widespread European countries, es-

pecially those that do not have such easily-accessible HPC facilities.



F1000 Research

Anyone who has never heard of F1000Research looks with a mix of curiosity and incredulousness at a peer-reviewed article that was published in a matter of days, featuring full information about the underlying data and a couple of carefully written expert reports displayed right next to the article. On the other hand, authors who have exploited this editorial model keep going back to it and recommending it to colleagues.

In the spirit of open science, F1000Research offers a transparent publishing platform to publish all forms of scientific research without editorial bias, from traditional research to study protocols, software tools and data descriptor articles. Its policies for transparency, open data and software have been highly influential in shaping the policies of major funding organizations, including the EU Research and Innovation programme.

While traditional pre-publication review models slow down the progress of research, publication at F1000Research is fast, with papers being published immediately, before entering the peer-review phase but clearly marked as such. F1000Research's publishing model combines the rapidity of pre-prints with cutting-edge publishing functionality that ensures the robustness, quality, reproducibility and transparency of its publications.

Originally, F1000Research's scope was limited to the life sciences. Today, it has become clear that open access and open science benefits all fields of research. The scope of F1000Research is now open to all, including medicine, making it attractive also for scientists working on problems and

F1000Research Open for Science

methods at the interface between the traditional scientific disciplines

The CompBioMed community will find much of interest in those articles that touch on their research. A few recent highlights are:

- Lost in translation [1], an article where Nachev, Rees and Frackowiak discuss how high-performance computing, combined with collections of large-scale data, enable the high-dimensional modelling that is critical to understand brain functioning and the translation of this knowledge to the clinical practice.
- On the evaluation of research software: the CDUR procedure [2], where Gomez-Diaz and Recio define, precisely but widely, the notions of research software and its authors and look closely at the evaluation issues, as the basis for the proposition of an assessment the CDUR procedure [version 2; peer protocol.

[1] Nachev P, Rees G and Frackowiak R. Lost in translation [version 2; peer review: 2 approved]. F1000Research 2019, 7:620

[2] Gomez-Diaz T and Recio T. On the evaluation of research software: review: 2 approved]. F1000Research 2019, 8:135

CompBioMed CoE Training: Winter School 2020 BSC, Barcelona, Spain

11-13 February 2020



The objective of this course is to give a panorama on the use of HPC-based computational mechanics in Engineering and Environment that the projects Barcelona Supercomputing Center are carrying out. This panorama includes the basics of what is behind the main tools: computational mechanics and parallelization. The training is delivered in collaboration with our Centre of Excellence.

A number of fixed value travel grants will be offered to selected participants to cover part of their travelling expenses.

More information: https://www.compbiomed.eu/training-3/

Upcoming Events Machine Learning meets Modelling and Simulation Methods

LRZ, Garching, Germany 16-18 March 2020



Within CompBioMed we have now dedicated a Work Package to the emerging topic of machine learning and artificial intelligence with a focus on high performance data analytics required for these approaches. This meeting will be an opportunity for Core and Associate Partners working on this topic to gather and discuss current progress, possibilities and needs to advance this growing field.

The agenda includes talks from people in the field and those looking to progress, followed by a day of software development sessions to advance the work and to learn from one another. A list of speakers is available on the CoE events page.

EuroHPC Summit Week

Porto, Portugal 23-27 March 2020



The EuroHPC Summit Week (EHPCSW) 2020 will gather the main European HPC stakeholders from technology suppliers and HPC infrastructures to scientific and industrial HPC users in Europe. As in previous years, PRACE, the Partnership for Advanced Computing in Europe, will organise the seventh edition of its Scientific and Industrial Conference (PRACEdays20) within the conference.

The main conference will take place from Tuesday to Thursday and will include a selection of plenary and parallel sessions. More information:

https://events.prace-ri.eu/event/937/ overview

CompBioMed CoE final review: Luxembourg

In November 2019, the first phase of our Centre of Excellence was concluded in the final review meeting with the European



Commission in Luxembourg. Attending the meeting we had at least one person from each of our partners and were able to pres-

ent all the work that had been conducted during the three years. Some highlights:

Development and testing in hospital setting of AngioSupport software by Life-Tec Group.

Palabos software from UniGe has improved parallelisation towards exascale performance for multi-physics applications of cardiovascular and other biomedical systems

- Alya software from BSC being used for clinical validation, new models and extending applications with improved efficiency.
- The use of machine learning for molecular dynamics (MD) simulations by UPF and Acellera
- Development of ensemble simulations for MD simulations from UCL et al. in collaboration with pharmaceutical companies (Janssen, Pfizer, GSK etc)
- Bone strength prediction pipeline from USFD linked with

Sheffield Hospital and tested by clinical staff

Alongside the research that has been taking place we worked hard to disseminate and reach a broad section of stakeholders and advance our training scheme. This included:

- 10 webinars reaching over 250 live participants and 1,500 YouTube views
- CompBioMed university education in medical school and biosciences department reaching over 300 students
- 85 publications
- Significant social media following (>700 twitter follow-. ers, >200 YouTube subscribers and >1 million twitter impressions)
- Award-winning and popular Virtual Humans video

We would like to thank all our Core and Associate Partners and all those people that we have collaborated with over the last 3 years for their support in making us a success and we look forward to the next 4 years.



Find CompBioMed online

Our website (www.compbiomed.eu) is full of all the latest news and information about CompBioMed, including further information on our Partners and Associate Partners, past and future events. We have an active and growing following on Twitter (@bio_comp), a user-forum on LinkedIn (Im CompBioMed) and we have our CompBioMed Coordinator: own YouTube channel (D Computational Peter V. Coveney (p.v.coveney@ucl.ac.uk) Biomedicine), where you can watch live streaming of events and presentations at our Virtual Humans film (https://youtu. the European Union's Horizon 2020 be/1FvRSJ9W734).

previous events and webinars, as well as This Centre of Excellence has received funding from research and innovation programme under grant agreement No 823712.

