Day 1 – Monday 29th April 2019 Mary Ogilvie Lecture Theatre, St Anne's College, Oxford		
09:00	Peter V Coveney, Blanca Rodriguez	**Welcome and introduction to AHM agenda**
09:15	Phil Fowler, Oxford	Predicting Antimicrobial Resistance: the role of computational modelling in translating genetics into clinical microbiology.
09:30	Andrew Richards	Diamond: Extracting and Managing Data behind the scenes
09:45	Vani Malyala, Sheffield	Modelling Cardiac Electrophysiology in Human Ventricular Tissue
10.00	**Invited Talk:** Stephen Payne, Oxford	Modelling the cerebral microvasculature across multiple length scales and multiple compartments
10:30	*Break/ Tea and Coffee*	
11:00	Alexandre Cabaye, Dassault Systemes' Biovia	Design of drugs targeting synaptic receptors with a combination of computational techniques
11:15	Dave Wright, UCL	Integrating binding affinity calculations into novel workflows
11:30	Peter Marinov, Oxford	The role of micro-structure heterogeneities in ventricular electrical conduction of ARVC patients.
11:45	Alfons/Gábor, UvA	HemoCell
12:00	Bettine van Willigen, LifeTec Group	AngioSupport: Interactive tool to support coronary intervention
12:15	Jon McCullough, UCL	Developments within HemeLB for the study of large-scale and multiphysics applications
12:30	Terry Sloan, EPCC	The HemeLB Offloader (Hoff)

12:45	Jenny Wang, Oxford	High-performance computer 3D modelling of cardiac electrophysiology for hypertrophic cardiomyopathy: the anti-arrhythmic effect of disopyramide
13:00	*Lunch*	
14:00	Alya Arabi, Zayed University	**Remote:** Mutations in DNA under the Effect of Electric Fields
14:20	Jazmin Aguado, BSC	High performance computing biomechanics simulations using Alya Red
14:35	Herman van Vlijmen, Janssen	Predicting Activity Cliffs with Free-Energy Perturbation
14:50	Joao Damas, Acellera	PlayMolecule: bridging the gap between researchers and biomedical applications in diverse computing infrastructures
15:05	Richard Clayton, University of Sheffield	Analysis of cardiac cell models using Gaussian process emulator
15:20	Andrea Townsend-Nicholson, UCL	Educating and engaging new communities of practice with high performance computing
15:35	*Break/Tea and Coffee*	
16:05	Jonas Latt, UNIGE	Progress in blood-flow modeling with the open-source solver Palabos
16:20	Adria Perez, UPF	Machine learning structural biology and drug design
16:35	Okba Hamitou, Bull	Exascale Architecture Co-design
16:50	*End of External Meeting*	
18:30	*Dinner: Pierre Victoire, 9 Little Clarendon Street Oxford OX1 2HP*	

Day 2 – Tuesday 30th April 2019
St Anne's College, Oxford

Parallel Sessions		
09:30		Innovation Advisory Board Meeting
09:45	General Assembly Meeting	
10:30	*Break/ Tea and Coffee*	
11:00	WP2/5/6 meeting	Innovation Advisory Board Meeting
13:00	*Lunch*	

14:00	WP3/4 Meeting	
15:00	*Coffee/Tea Break*	
15:30	WP1: Emily Lumley	Project Management
15:40	WP2: Mariano Vazquez	Biomedical Research Activities
16:00	WP3: Manuela Corsini and Hugh Martin	Training and Dissemination
16:20	WP4: Gavin Pringle	Innovation and Sustainability
16:35	WP5: Marco Verdicchio	Resource and Infrastructure Support
16:50	WP6: Alberto Marzo	Empowering Biomedical Applications
17:15	*Meeting Ends*	

Phil Fowler

The growth of antimicrobial resistance (AMR) is widely recognised as a threat to much of modern medicine and **a** likely cause of many additional deaths worldwide in the coming years. To determine the suitable antibiotic to treat a serious infection, standard clinical practice is to culture a sample and then examine how well the bacterium grows in the presence of a number of different antibiotics. Whilst much progress has been made automating and miniaturising this process, it remains expensive, moderately slow and often not very reproducible. In the last five years, there has been a global push to replace culture-based clinical microbiology with whole genome sequencing where the patient sample is directly sequenced, and the genome of the pathogen is examined for mutations known to confer resistance to specific antibiotics. Whilst laudable, one key weakness of this approach is it is inferential so cannot return a result when a rare or novel genetic variant is encountered. In this talk I will describe the progress we have made in developing computational methods, including binding free energy prediction and machine learning, to predict *de novo* the effect of genetic variants on the action of specific antibiotics on *S. aureus* and *M. tuberculosis*.

Andrew Richards

This talk will briefly describe what happens behind the scenes at Diamond during an experiment in terms of acquiring, processing, and managing the ever-increasing data volumes being created by experiments today. It will also look to the future and discuss Diamonds plans to provide services in the cloud to enable researchers to continue to analyse data away from Diamond and how its users can play a vital role in shaping how Diamond develops its next generation of data analysis services.

Sathyavani Malyala

The heart is a vital organ that pumps oxygenated blood to the whole body with repeated rhythmic contractions, and continued heart beats are essential for the body to survive. The heart is an electromechanical pump, the electrical activity of the heart acts to trigger and synchronise mechanical contractions. Cardiac arrhythmia is an irregular rhythm caused by abnormal electrical activity. When there is a disturbance in the propagation of electrical activity in the heart, the electrical wave breaks forming abnormal electrical activity called re-entry. In re-entry, the activation wavefront breaks, so that the wavefront is able to continually propagate into recovered tissue. Re-entry is dangerous because the activation rate is higher than the resting heart rate, so normal pace making activity is suppressed. Ventricular fibrillation (VF) is a severe

arrhythmia (several re-entrant waves) where the normal electrical activity is completely disturbed which results in little or no mechanical contractions. Experimental studies show that VF is associated with re-entry.

Hypertensive heart disease causes diffuse fibrosis in ventricles and studies shows that they can act as a source of anatomical re-entry. It can be very hard to study the effect of fibrosis of certain size in experiments so computational models of cardiac cells integrated in cardiac tissue models are useful to study vulnerability of re-entry. This study uses Gaussian random field to generate sample of smooth variation of diffusion coefficient mimicking diffusive fibrosis of certain radius. This study will be very useful to find the effect of diffusive fibrosis (in ventricles) on the vulnerability of re-entry in both 2D and 3D.

Stephen Payne

In our previous work, we have developed a number of different models of the cerebral circulation, from 0D lumped compartment models to highly detailed 3D models of the microcirculation. Through the use of homogenisation techniques, we have been able to scale up the microcirculation to a single compartment porous medium model that couples with models of individual penetrating cortical vessels. In the first part of the talk, I will present our current work that expand this through the use of a multiple-porosity porous medium model in order to model the cerebral cortex more accurately. This work also directly links to multiple-compartment poro-elastic models, developed by a number of groups, which I will discuss. In the second part of the talk, I will present our current work on bridging the length-scale gap between large vessels (i.e. those that can be individually imaged) and the microcirculation, over which length scales surprisingly little anatomical information is known. I will present our proposed modelling approach and discuss how such whole-brain blood flow models can be validated and used within a patient-specific model, in particular in response to ischaemic stroke, but also with regard to the ageing brain.

Alexandre Cabaye

Glutamate is the major excitatory neurotransmitter in the Central Nervous System (CNS). It activates ligand gated ion channels (iGluRs) and G-protein coupled receptors (mGluRs). The former secure fast synaptic transmission whereas the latter modulate that event allowing its fine-tuning. Thus, metabotropic glutamate receptors (mGluRs) are actively investigated as potential therapeutic target for several CNS diseases and disorders (e.g. Parkinson's disease, depression, anxiety, schizophrenia, epilepsy and pain). In this context chemo-informatics tools help us to rationally design and optimize drugs for group III mGlu receptors, by the combination of known methods from homology modelling and docking, all the way up to large scale molecular dynamics and metadynamics.

Dave Wright

Binding Affinity Calculator (BAC) is a flexible tool for computing the strength of drug binding to target proteins using molecular simulation. An increasing number of projects we are involved in deploy it as part of larger workflows, including those integrating predictive modelling with machine learning and those designed to evaluate the fidelity of our simulations. In this talk we describe our experiences working with back in these environments.

Tim Van den Boom,

Every morning, a cardiac team needs to discuss the treatment of multiple patients with coronary artery disease (CAD). These patients have one or multiple severe occlusions in the coronary arteries and for each patient a choice has to be made between coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI). This choice is currently based on studying the coronary angiogram and the experience of the cardiac team. However, in case of multiple occlusions, diffuse coronary disease or complicated vasculature, it may be difficult to determine in the position, length or diameter for a CABG or PCI can become very difficult.

Therefore, we developed an interactive model that can predict the outcome of CABG or PCI to support clinical decision making of coronary interventions. By extracting the coronary geometry from the coronary angiogram, one-dimensional CFD simulations allows the calculation fractional flow reserve (FFR). The interactive model then allows the cardiologists to perform interventions and calculate the post-FFR.

Jon McCullough

This talk will discuss recent developments within the HemeLB lattice Boltzmann code that have occurred at UCL. Three distinct areas will be presented. Firstly, we will articulate the process for coupling HemeLB with other codes and in particular with itself. Secondly, the incorporation of colloids within the HemeLB code for the study of magnetic drug targeting (MDT) will be outlined. Finally the scaling and performance of the code on machines with O(100,000) processors will be discussed.

Terry Sloan

This presentation outlines an approach for enabling access to HPC applications as Software as a Service (SaaS) on conventional high-end HPC hosts such EPCC's Cirrus and cloud providers such as Microsoft's Azure service. The focus for the approach is enabling access to the HemelB application with the Polnet biomedical workflow. The presentation will report on an implementation of this approach that allows Polnet workflows to run on the Cirrus and LISA supercomputing services at EPCC and SURFsara respectively.

Alya Arabi

External factors such as intercalators, radiations, and electric field can trigger higher rates of mutations. This work is an investigation of the effect of electric fields on point mutations in DNA, a mutation mechanism introduced by Löwdin. Results from DFT calculations on the gas phase base pairs showed that the mutation is more likely to occur in the GC base pair than the AT base pair even in the presence of the strongest fields applied, 10^9 Vm^{-1}. The mutation in the AT base pair is mainly through tunnelling, irrespective of the strength of the field applied. Results from MD simulations, followed by QM/MM optimizations on a solvated dodecamer DNA (depicted in the Figure below) showed that fields at various strengths and applied in three different directions cause at least one of the following effects: (a) a decrease in the barrier height of the double proton transfer reaction, (b) a shift along the reaction coordinates, and (c) a flip from an asynchronous to a synchronous reaction.

Jazmin Aguado-Sierra

In this talk I will present some of the latest results on the use of Alya red to create simulations to study the human cardiac physiopathology. Preliminary results on the study of ventricular tachycardia will be shown and discussed.

Herman Van Vlijmen

Activity cliffs (ACs) are an important type of structure-activity relationship in medicinal chemistry where small structural changes result in unexpectedly large differences in biological activity. Being able to predict these changes would have a profound impact on lead optimization of drug candidates. Free-energy perturbation is an ideal tool for predicting relative binding energy differences for small structural modifications, but its performance for ACs is unknown. Here, we show that FEP can on average predict ACs to within 1.39 kcal/mol of experiment (~1 log unit of activity). We performed FEP calculations with two different software methods: Schrödinger-Desmond FEP+ and GROMACS implementations. There was qualitative agreement in the results from the two methods, and quantitatively the error for one data set was identical, 1.43 kcal/mol, but FEP+ performed better in the second, with errors of 1.17 versus 1.90 kcal/mol. The results have far-reaching implications, suggesting well-implemented FEP calculations can have a major impact on computational drug design.

Joao Damas

Development of computational methods in the biomedical area is thriving, particularly in molecular medicine. The rate for these state-of-the-art methods to reach the researcher (i.e. the end user) and impact research is still low, which bottlenecks the speed of identification of new targets and development of new drugs. Building robust pipelines and efficient workflows from the computational methods and making them easily available to the researcher has been one of the objectives of the PlayMolecule platform we've been developing. PlayMolecule aims to bring easy-to-use and intuitive applications that can work from anyone's web browser and run on diverse computing infrastructures from small computer clusters to HPC, without any necessity to know about the infrastructural details behind it, which allows the researcher to focus on their research projects.

Andrea Townsend-Nicholson

In my role as UCL training lead for CompBioMed, a H2020 Centre of Excellence in Computational Biomedicine (compbiomed.eu), and as Head of Teaching for Molecular Biosciences at UCL, I have led the development of HPC-based education targeting medical students and undergraduate students studying biosciences in a way that has explicitly designed to be integrated into their existing university programmes. One version of this course has been designed for medical students in Years 1 and 2 and one of the unique features of the course is the integration of clinical and computational aspects, with students obtaining and processing clinical samples and then interrogating the results computationally using code that was ported for the first time to HPC, at CompBioMed's HPC Facility core partners (EPCC, SURFsara and the Barcelona Supercomputing Centre). Another version of the course replaces the final year research project course for undergraduate science students, providing the opportunity to develop and pursue experimental hypotheses that involve the integration of experimental and computational methodologies. In the past two years these courses have successfully run with 60 medical students and 195 biomedical science students participating. Our experience has enabled us to distil our methodology into an educational template that can be delivered at other universities in Europe and worldwide.

Adria Perez

Abstract: Modern machine learning algorithms bring novel ways to create powerful data-driven predictive models to aid in drug discovery. Our work has been focused in harnessing the recent innovations to develop novel tools for drug discovery. Here we present our most recent applications and show their performance.

Okba Hamitou

The Exaflopic challenge is complicated due to the fact that the number of nodes is very high. For instance, ten thousand nodes are required for reaching the hundred petaflops which should be reachable by horizon 2022. The second challenges are the energy consumption and the storage solution which are high and need to be managed efficiently. From the end-user point of view, the challenge is to take fully advantage of the performances provided by new CPUs; mainly, application developers need to be able to provide fully vectorized applications.