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Multiscale modelling and simulation: a position paper

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Introduction

Many if not all of the quantitative research challenges in highly topical contemporary issues, such as climate, energy, materials, sustainability, ecology, health and disease, urbanization, economy, finance, psychology and sociology require in one way or another an understanding of multiscale systems [1–3]. Likewise, in engineering and manufacturing, designing and controlling systems have to take into account their multiscale character [1,4,5]. In short, multiscale modelling is ubiquitous, so that progress in most of these subjects of pressing societal concern is determined by our ability to design and solve multiscale models of the particular systems under study. In our opinion, systems science is nothing other than the study of multiscale phenomena in the domain of interest, where understanding of the phenomenology turns critically on our ability to represent or account for interactions from multiple levels. Systems biology and systems medicine are but examples of this kind. One might bear in mind Sydney Brenner's famous aphorism about the need to model 'from the middle out' to indicate that there is no preferred level at which a description of a system should be furnished—it depends on what phenomena one wishes to describe [6].

Notwithstanding many important successes, we believe that the field of multiscale modelling does have a number of relevant open questions that, although they are deemed important and sometimes critical for the development of the field, have so far been hardy explored. This was a very important conclusion of the workshop Multiscale Modelling and Computing that was held from 8 to 12 April 2013 in Leiden, The Netherlands.1 This discussion paper expresses the consensus expertise opinions as reached during that workshop and explores these open questionsin the field of multiscale modelling and simulation.

This paper is not a review of the field, nor does it attempt to be all-inclusive. However, given the breadth of expertise of the participants at the Leiden meeting, from many different fields of science and engineering, we believe that this article does represent widely shared opinions and identifies some important open and unresolved issues within the field of multiscale modelling and computing. We hope that this short contribution may serve to lay the foundation for new and further intensified *multidisciplinary* research efforts, cutting through the many scientific domains concerned, aiming at those open questions identified here.

The breadth and depth of multiscale modelling

Multiscale modelling is an actively pursued approach to make sense of wide ranges of phenomena, both natural and anthropogenic. In many different communities, impressive results can be presented. In some areas of complex fluids and materials science [4,5,7–11], or applied mathematics and numerical analysis [1,3,12–14], the field has already reached a level of some maturity, for example including 'classical' methods/algorithms, such as homogenization [1]. For other fields, such as, for example, the biomedical [15–20] and the socio-economic domains [21], multiscale modelling is still relatively new. However, in most if not all cases of concern, the research and associated funding to pursue such studies are confined within the boundaries of individual scientific and engineering disciplines. In our view, this renders the field unnecessarily disparate and fragmented. Indeed, it has already led to a slowing down and even stagnation in many relevant topics, to reinventing the wheel, to confusion with respect to terminology and concepts, and to sub-optimal solutions for the implementation of production mode multiscale models running on state-of-the-art computing infrastructures.

Genuine synergy between communities at large not only is possible, but also highly desirable if not essential, for multiscale modelling is almost intrinsically multidisciplinary. When coupling processes at different spatio-temporal scales, in many cases different types of physics, chemistry, biology, physiology, ecology, epidemiology or even socio-economic processes need to be coupled together. Barely anyone in this era of increasing specialization can pretend to have an appropriate let alone complete understanding. Moreover, well-established numerical analysis, theories and standard modelling approaches need to be reformulated or adapted for novel multiscale modelling challenges.

The main topics that in our view would benefit from a targeted *multidisciplinary* research effor are related to reaching consensus on what exactly we mean by 'multiscale modelling' and the

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terminology that is used, on formulating a generic theory or calculus of multiscale modelling, including scale bridging methodologies, on applying such concepts to the urgent question of validation and verification of multiscale models, as well as developing formal mathematical approaches appropriate to address the issue of error propagation in, and convergence of, multiscale models. Moreover, we believe that this would, in principle, lay the foundation for more efficient, well-defined and usable multiscale computing environments. In §§3–7, we will further discuss these topics. We believe that an investment in these topics would be timely and would result in a strong boost to the application of multiscale modelling in specific scientific domains. We also strongly believe that, although many of the topics that we identify could, in principle, be tackled within the boundaries of specific disciplines, a cross-disciplinary investment would be much more beneficial to the field at large.

Note that definitions we will use in the rest of this paper for multiscale, single-scale models, and other terminology are those given in the paper by Chopard *et al*. [22] in this Theme Issue.

What is multiscale modelling?

Basic questions such as 'what is a multiscale system?', 'what do we mean by multiscale modelling?' and 'how could a multiscale model be developed?' immediately lead to many different views; see [23] for one example. We found that this is partly because of the lack of a common terminology. Researchers do not agree on basic definitions and terminology, the same word meaning very different things to different communities. Examples include 'fully resolved models', 'single scale models', 'fine-grained models', 'microscopic models' and so on. They sometimes mean the same thing, but can also have quite different meanings, depending on communities. But this also relates to different views on what exactly a multiscale model is or how a multiscale model is to be developed. Agreement on terminology and methodology would be extremely beneficial, to avoid confusion, to better understand and benefit from developments in different fields, and to foster cross-disciplinary research.

A closely related issue is that of the classification of multiscale models. A number of different taxonomies exist (e.g. the widely used but certainly not universally adopted 'serial' versus 'concurrent' [24]). During the workshop, three different but partly overlapping classifications where introduced [4,25–28] and others exist [12,24,29,30]. A shared view on multiscale modelling and a clear, all-inclusive, and universally adopted classification would be very beneficial to the field of multiscale modelling. This would facilitate better sharing of ideas and research and allow for more straightforward collaboration across disciplines.

What is a scale? And when is a model multiscale? Spatial and temporal scales are probably

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clear. But what about other, maybe more abstract scales? For instance in economic models, the flow of money or goods could connote a scale, with processes influencing each other but trading on large and small scales. Are scales correlated? In many examples from physics or engineering, the spatial and temporal scales seem to be correlated (micro–meso–macro, both in time and space), but when shifting focus to the life sciences and biomedical systems this is not necessarily always the case [20]. Deeper reflections and analysis of such questions are required.

To summarize, in our view we need a theory of multiscale modelling. Much like a generic theory of for instance linear second-order partial differential equations (hyperbolic versus parabolic versus elliptic, and all related theory and numerical analysis), some formal and generic mathematical theory of multiscale modelling is needed, which should be independent of specific domains and applications. This 'calculus of multiscale modelling' should then allow us to formalize the field, to study the properties of our models, including the issue of scale bridging and error analysis (see following sections). Finally, one could even hope that such theory, in combination with many examples of successful multiscale models could also lead to best practice in multiscale modelling, leading *inter alia* to 'cook books' of multiscale modelling and simulations.

At the core of a multiscale model are models and related algorithms to couple together processes at different scales, to transform information at one scale and transfer it to another scale. We call this *scale bridging*.

Scale bridging should be an important part of a theory of multiscale modelling. Many scale bridging methods are known, some are being improved, but they invariably depend quite strongly on specific application domains. Examples are sampling, projection, splitting, lifting/upscaling, homogenization/coarse graining, refinement, micro–macro coupling, constitutive models, boundary methods, etc. [1,3,7,12,29,31]. An important question is whether we can reduce all these scale bridging methods to a few generic classes, a suggested in for example [27,28]. For instance, in many applications, particle methods acting on the micro-scale (such as molecular dynamics or dissipative particle dynamics) are coupled to continuum methods acting at the macro-scale (e.g. finite-element methods in say structural or fluid mechanics) or to other coarse-grained particle methods at the meso-scale, as for example in [7]. These observations suggest that it should be possible to formulate generic scale bridging methods. We believe that this should lead to better understanding of our multiscale models (for example, in terms of error propagation, or creating optimal computing environments, see following sections), and could also help in better formulating boundary conditions and initial conditions in the presence of scale bridging.

More fundamental questions can also be asked. Can we find underlying theories that allow us to formulate scale bridging methods, such as the Mori–Zwanzig formalism [32]? And how do the underlying physics, chemistry, biology, etc., influence the way in which processes can be coupled together? Are there a minimal set of conservation laws for scale bridging?

Finally, on a more practical level, important yet unresolved questions address how scale bridging methods compare, and what their effect is on the accuracy of multiscale models and on the efficiency of simulations based on these.

Validation, error propagation, verification, consistency

With a few notable exceptions (e.g. [33]) a largely unexplored area in multiscale modelling seems to be that of validation of multiscale models, error propagation, verification and consistency. A few convincing examples of numerical analysis applied to multiscale models, with clear theorems on convergence and consistency are published [12,13,34,35]. Also, inspired by the work of Prof. T. Oden and co-workers some very powerful techniques that could be of general value for consistency and error analysis for multiscale modelling were discussed [36–38]. However, these examples and techniques have not yet found their way into other disciplines.

In relation to the aforementioned lack of a theory and methodology for multiscale modelling, we certainly need a calculus for validation, error propagation and consistency of multiscale modelling. The hope is that, by formulating mathematically rigorous theories of multiscale modelling, formal and well-founded approaches to error analysis of multiscale models should emerge. A related avenue to explore is 'coupled numerical analysis', the idea being that if we assume that we understand how to do numerical analysis on a single scale model, could we use that knowledge to analyse coupled models?

Validation and uncertainty quantification, as well as sensitivity analysis of multiscale models [33] should also be much better understood and put into practice. We need benchmark results, perhaps stemming from fully resolved models, that can be used to 'calibrate' parameters of multiscale models and then, based on uncertainty quantification and sensitivity analyses, seek to put estimates on the quality of predictions that we make with our multiscale models.

A clear conclusion is that all researchers agree on this set of issues. However, hardly any group has really taken up the major challenges posed. A cross-disciplinary programme of work, involving interdisciplinary community effort, cutting through application domains, could prove highly beneficial in addressing these very important issues.

A possible approach

Over the past few years, we have published a series of papers in which we formulated a

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framework for multiscale modelling [17,20,25,27,28,34,35,39–41]; see also the contribution by Chopard *et al.* [22] in this Theme Issue. This framework starts with the notion of defining a multiscale model as a collection of single scale models, coupled via scale bridging methods. By assigning clear scales to the single scale models, a multiscale model can be mapped to a scale separation map, with directional edges between the single scale models representing the scale bridging methods. By observing the relative placement of single scale models on such a map, and taking into account the nature of the resultant graph that is built up from the single scale models and the scale bridging connectors (basically, whether the graph is cyclic or acyclic) a high level but quite strong classification of multiscale models emerges. Moreover, such a scale separation map itself is in a way already a powerful methodology to design and reason about multiscale models. Next, by assuming a generic execution loop for each single scale model, and assigning very basic operators (that take care of processing the dynamics of a single time step in a single scale model, of handling boundary conditions, and of observing the state of a single scale model), it turns out that only a very few different types of multiscale couplings are possible. This framework actually laid the foundation for a multiscale modelling and computing environment and by now has been shown to be very effective for multiscale applications from a large variety of domains [42]; see also §7.

In the light of the previous discussions, we now briefly conjecture as to how our framework could help in filling in the open questions identified and discussed in the previous sections. First, the scale separation map seems to provide an important conceptual basis for multiscale modelling, going way beyond a simple visualization of the model in hand. One could add more axes, representing other scales or dimensionalities of single scale models, thus revealing more structure in multiscale systems and possibly leading to a broadly agreed classification.

Moreover, as the scales are made explicit, a 'distance' between single scale models on the map should contain information on modelling errors, perhaps in combination with the abstraction in the terms of the high-level operators in the execution loop, thus forming a starting point for a calculus of multiscale errors. For instance, for a specific example of a reaction–diffusion system, we applied this approach and were able to find expressions for the scale-separation error as a function of the 'distance' between the single scale models on the scale map [35]. We believe that such an approach could serve as a starting point for all issues discussed in §7.

This framework could also help in formulating a more fundamental theory of scale bridging methods. The framework suggests that on a sufficiently high enough level of abstraction only a very few different methods exist in which scales are coupled to each other. As with the scale map, it would then be quite tempting to take this high-level classification as a starting point for exploring possible emerging structures in all the variety of scale bridging methods that were

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mentioned in §4.

Multiscale computing

The final topic that received considerable attention during the Leiden workshop was that of multiscale computing and software environments that facilitate multiscale modelling and simulation. In the majority of cases, a multiscale simulation comprises two or more models at specific scales coupled together using some scale bridging technique. Depending on the type of multiscale model, the execution order of the single scale models may differ but, in the final analysis, developing efficient multiscale simulations is all about coupling codes together via scale bridging algorithms. Another observation was that in many cases the single scale models are well-established methods (e.g. molecular dynamics) and that existing software packages are used (e.g. GROMACS) that implement them. Therefore, developing a multiscale simulation in many cases boils down to developing software to glue together existing pieces of software that implement single scale models and scale bridging methods.

These observations suggest that frameworks for multiscale modelling and simulation would be very beneficial to the community, and some were presented during the workshop (e.g. [39, 42–44]). Many more environments do exist, some not necessarily tied to multiscale models, others specifically developed for multiscale modelling and simulation [5,8,45,46]. So far, many of these frameworks seem to be quite pragmatic. We certainly need frameworks supported by underpinning theory. This would result in generic frameworks with much added value for specific domains. Also when coupling more than two codes together, powerful generic frameworks, supported by theory, would help a lot in developing, debugging and maintaining multiscale modelling software.

Such environments should contain scale bridging frameworks, and interchangeable components to foster comparison (e.g. replacing one single scale code by another, implementing the same model). Moreover, they should contain large collections of benchmark problems and databases to compare and calibrate models.

Another important and far from trivial issue is the actual execution of multiscale simulations. In principle, we want to be able to execute our models on any system, ranging from a laptop to high-end peta-scale systems, and anything in between, in any combination as required or desired, all depending on the computational needs of the simulation. In principle, some existing multiscale modelling and computing environments do support many types of computational infrastructure, but here too community wide efforts would be beneficial to develop highly efficient and re-usable environments. Moreover, especially when targeting high-end computers, and/or when requiring

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non-standard access to these computers (e.g. for distributed computations, or when needing advanced reservations and co-allocations) not only technical hurdles need to be overcome, but also the way such systems can be accessed needs to be brought into line with the requirements of multiscale computing. As became clear during the Leiden workshop, some typical issues in for example access policies to European e-Infrastructures are a true obstacle for multiscale computing. It should be a source of embarrassment to all that the *modus operandi* of most supercomputers has barely changed in the 40 or so years since these resources became available for scientific research.

To conclude

Notwithstanding some notable successes, in our opinion, the field of multiscale modelling does have a number of unresolved questions that, although they are deemed important for the field, have so far hardly been explored. Given the importance of multiscale modelling for so many fields of science and engineering, we believe that targeted and substantially funded *multidisciplinary* research efforts are urgently needed. We should reach consensus on what exactly we mean by multiscale modelling and the terminology that is used; we should formulate a generic theory or calculus of multiscale modelling, including scale bridging methodologies; we should apply such theory to the urgent question of validation and verification of multiscale models; and we should develop formal mathematical approaches to the issue of error propagation in, and convergence of, multiscale models. Moreover, we believe that this would, in principle, lay the foundation for more efficient and well-defined multiscale computing environments. We observe that such fundamental cross-disciplinary research in multiscale modelling and computing is currently not well addressed by funding agencies, which contributes in part to the fragmentation we seek to redress. We believe that research to fill the gaps as identified in this paper is timely, highly relevant, and with substantial potential impact on many scientific disciplines.

We should act now!

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