From advanced aircraft design to drug delivery

Manufacturing shock interactions for innovative nanoscale processes

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The sonic boom of aircraft has been known since the early days of supersonic aviation. It both fascinates and frightens mankind, even today. Put simply, a flying object that moves faster than the air in front of it can be pushed away causes a very strong and fast compression of the air. This compression manifests as a sonic boom on the ground when the object moves at supersonic speed.

Jumping to biomedical engineering, consider the non-invasive treatment of kidney stones. By using extracorporeal shockwaves, patients can be treated with lithotripsy to pulverise hard tissue material and allow for its natural elimination. These two seemingly wholly different examples share the same underlying physical mechanism, the effects of compressibility in fluid flow.

Fundamental research on the outlined phenomena is still needed to optimise engineering applications, deliver novel medical treatments, and discover new phenomena and physical mechanisms. Academic research often appears to address generic or abstracted problems, yet the value of these scientific results is easily underestimated. The study of shockwave interactions with an isolated gas bubble, although hard to grasp, improves physical understanding. Understanding and controlling related phenomena stimulated new strategies for gene therapy in vivo (sonoporation), extensions of which are currently actively investigated.

NANOSHOCK

The objectives of the 'NANOSHOCK' research project aimed to provide computational methods for fundamental physical discovery to study shockwave-driven phenomena and exploit their technological potential. The main research question is how to manufacture shock interactions for innovative nanoscale processes. That includes the defined generation and control of shocks in complex environments, like living organisms, to design drug delivery techniques with high precision while minimising side effects. These goals are tackled through quantitative and predictive numerical simulations using 'state-of-the-art and beyond' computational methods.

Supported by benchmark quality experiments, NANOSHOCK adds value to the scientific and engineering community in sharing its paradigms and most advanced generalised simulation framework for compressible multiphase flow problems. We have identified a novel injection mechanism for layered capsules near tissue-surrogate material that has the potential to boost targeted gene therapy. Moreover, the generated simulation capabilities allow many other engineering applications to be studied, such as shock-induced droplet fragmentation or classical bluff body analysis in compressible flows. This is where our research closes the circle from understanding to technology—starting from a complex problem, fundamental research creates methodologies to solve the objectives and simultaneously stimulate novel application concepts for both the developed methods and the discovered physical mechanisms.

During the NANOSHOCK project, we have focused mainly on canonical configurations, i.e. generic settings representing real applications in their governing physical domains. For example, the isolated collapse of a single or multiple gas bubble near a compliant interface by the effect of a passing shockwave mimics the underlying process during lithotripsy. Detailed simulations of this problem reveal the limitations and potential of the prevailing mechanisms. The challenge of modelling such processes numerically is due to the multi-scale nature of the problem. On the one hand, density changes across phase interfaces and sudden pressure increase by a shockwave occur on extremely small spatial and temporal scales and imply the need for very high resolutions of the underlying computational mesh on which the physical solution is approximated. On the other hand, although initiated by the very quick shockwave passage, the actual observable dynamics in terms of flow evolution or interface deformation happen on a much larger spatial and temporal scale and necessitate large simulation time intervals. For example, consider an underwater detonation. After ignition, a far-distant observer will hear and experience the generated shockwave almost instantaneously. But only seconds or minutes later, the resulting effects of a huge water splash and wave motion will appear. Therefore, a virtual deterministic experiment needs to capture both scales and requires very efficient computational methods. This short excursion shall clarify the complexity and cost (in terms of computational resources) of numerical predictions for compressible multiphase problems.

ALPACA: a numerical simulation environment

A key NANOSHOCK result was the development of the numerical simulation environment "ALPACA". With 20,000 lines of code, ALPACA is one of the most advanced simulation environments for large-scale laboratory simulations of complex fluid flows. We have developed ground-breaking numerical methods with unprecedented accuracy and efficiency, developing a virtual flow-physics laboratory. ALPACA is open source (https://gitlab.lrz.de/nanoshock/ALPACA) and available to the scientific community. It is modular, so it can be adapted and extended to integrate any flow-physics model based on continuum conservation equations. A range of post-processing tools and data analysis instrumentation are also available.

The backbone of ALPACA is an advanced wavelet-based multi-resolution method for simulating compressible multiphase flows. Phase interfaces are sharply represented by level sets that indicate the exact distance of a fluid element to the separating manifolds of different materials. So-called low-dissipation high-resolution methods are employed for

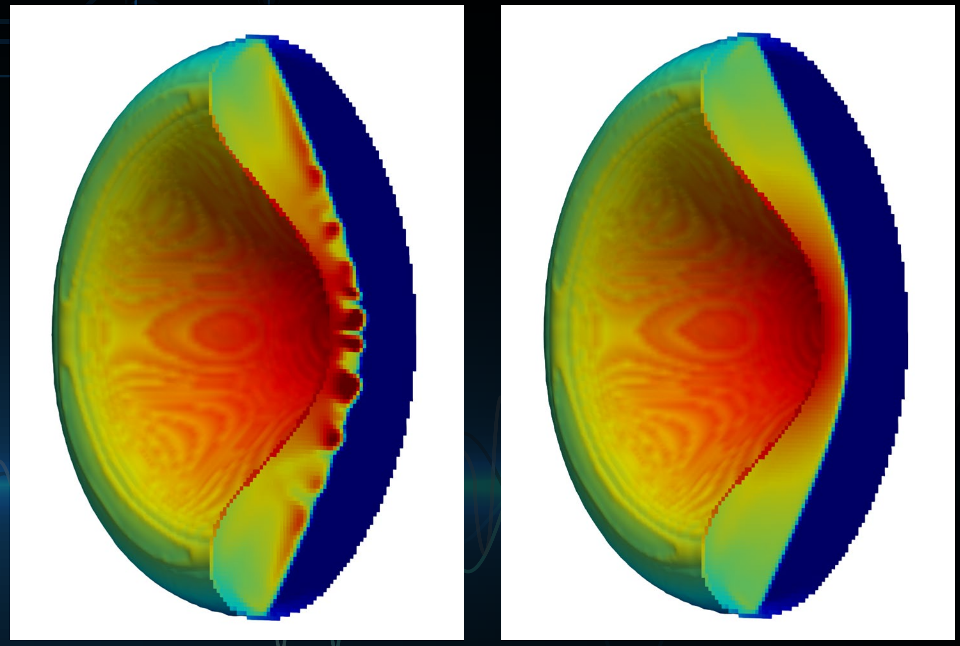

Figure 1: A 3D shock interface interaction of an air bubble in water: velocity magnitude within the air bubble from blue = 0 to red = 3,500 at t=2.6x10^{-6}. Original HLLC result showing carbuncles (left) vs. modified HLLC-LM (right) using 160 cells per air bubble diameter (reprinted with permission from Elsevier: Fleischmann, Adami and Adams, 2020).

direct simulations. Surprisingly, although the discipline of computational fluid dynamics (CFD) for the depicted problems is more than four decades old, there is still today no scientifically agreed universal method available. Further methodological ground-breaking improvements are expected before CFD for such very complex applications can be considered above technology readiness level (TRL) three (research to prove feasibility).

Coping with 'carbuncles'

As an example of an important achievement with regard to the computational modelling, we present here our solution strategy to cope with the long-standing problem of 'carbuncles', the 'greatest unresolved problem of classical finite-volume schemes' (van Leer, 2009).

Carbuncles are classified as numerical shock instabilities that occur in solutions to the compressible Euler equations. Originally, it was believed that the advanced HLLC Riemann solver could suppress this artificial phenomenon.

> We have used ALPACA to investigate various shock-induced multiphase phenomena like the transient perforation of biomaterial.

Later, however, it was found that the carbuncles still occur for today's achievable and routinely employed high spatial resolutions. Figure 1 shows the deformation of a gas bubble after exposure to a shockwave; see the left plot for a visualisation of the carbuncles that falsify the velocity profile. Obviously, the carbuncle-triggering error in the scheme was only suppressed but not eliminated.

As typical for the scientific evolutionary advancement, novel capabilities and achievements challenge previous understandings and require new research. For the example of carbuncles, the progress in computer science allows the simulation of complex compressible flows at an unprecedented level of detail, which in turn questions the putative solution strategies. Through elaborate fundamental numerical method development, we have found and proposed a solution to the carbuncle phenomenon by a simple modification of the approximate Riemann solver class (like HLLC), see Figure. 1 (b). Interestingly, contrary to the intuitive approach of adding damping mechanisms when undesirable disturbances show up, here, the damping or 'dissipation' perpendicular to the shock motion is reduced to heal the carbuncle phenomenon (Fleischmann *et al.*, 2020; Fleischmann, Adami and Adams, 2020).

Cell perforation

Besides the accomplishments in advanced numerical method development, we have used ALPACA to investigate various shock-induced multiphase phenomena like the transient perforation of biomaterial. A highlight result was the study of the interaction and penetration of liquid-liquid material interfaces initiated by the shock-driven collapse of single and multiple microbubbles situated near the material interface (Figure 2, Pan *et al.*, 2018). This generic surrogate model was shown to adequately represent the relevant physics of sonoporation, the perforation of living cells by microbubble collapses.

We were able to demonstrate the phenomenological effects of process-parameter variations. Shock overpressures were identified where an adverse continuous perforation occurred, in contrast to the desirable effect of a confined puncture allowing for self-healing effects.

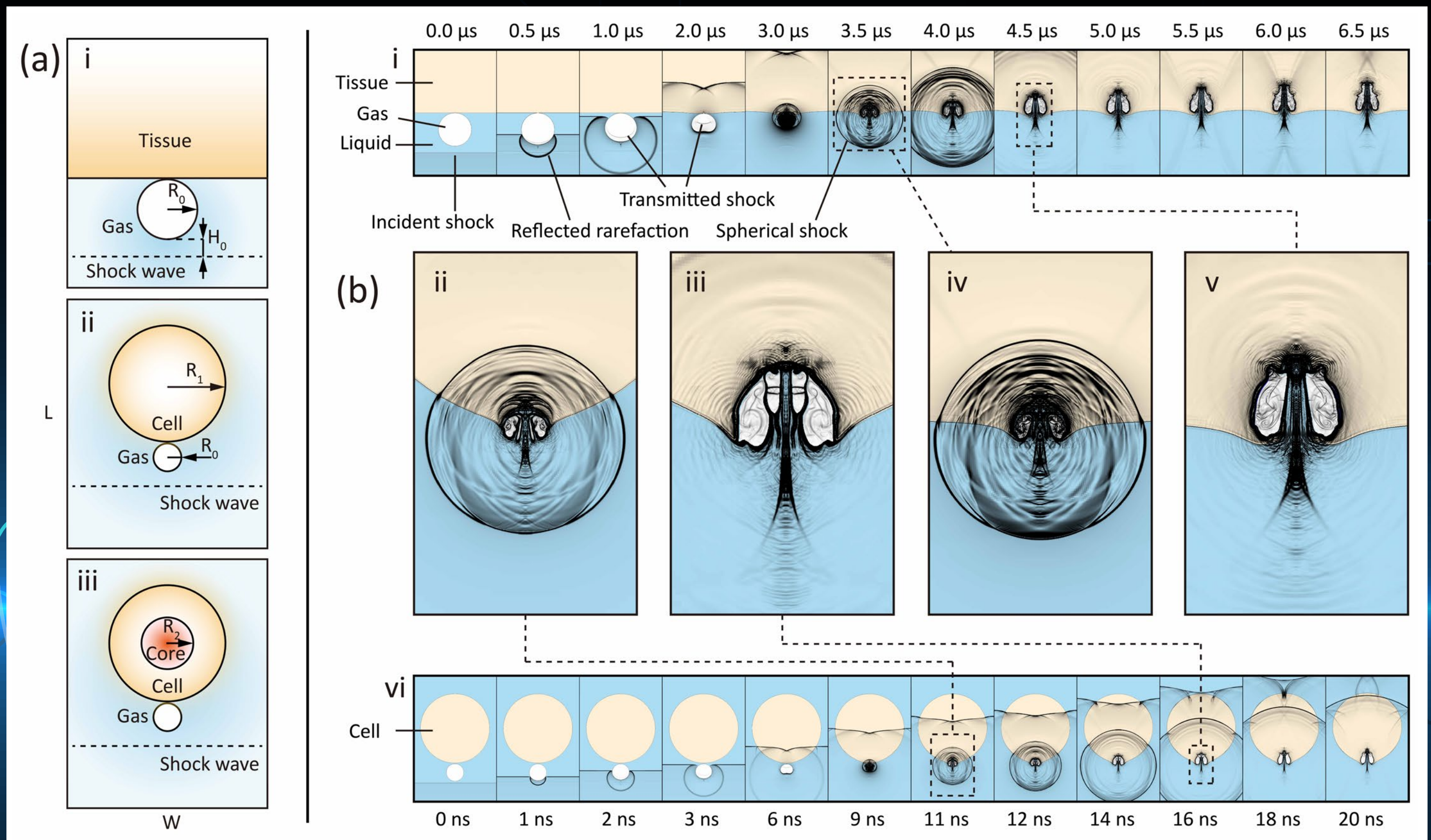

Figure 2: Surrogate models for the numerical simulation of sonoporation (taken with permission from Pan et al., 2018).

Wide-ranging applications

Physical discovery is one part of the successfully completed NANOSHOCK research project; the other is making one of the most advanced virtual environments for laboratory simulations of complex fluid flows available to the research community. While further stimulating ground-breaking research on novel microinjection techniques, the outcome of the 'catalytic' ERC funding allows us to address various other research fields and industrial applications, facilitating new technological opportunities.

> We have initiated new collaborations in the fields of nanoparticle generation, droplet disintegration at extreme energies, surface cleaning and additive manufacturing.

More than 20 peer-reviewed journal publications have emerged from the NANOSHOCK research group, and we have reported our developments at many scientific conferences.

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PROJECT NAME

NANOSHOCK - MANUFACTURING SHOCK INTERACTIONS FOR INNOVATIVE NANOSCALE PROCESSES

PROJECT SUMMARY

The 'NANOSHOCK' research project aims at providing computational methods for fundamental physical discovery to study shockwave-driven phenomena and exploit their technological potential. The main research question is how to manufacture shock interactions for innovative nanoscale processes. That includes the defined generation and control of shocks in complex environments such as living organisms to design drug-delivery techniques with high precision while minimising side effects. These goals are tackled by means of quantitative and predictive numerical simulations using the latest and novel computational methods.

PROJECT LEAD

Nikolaus Adams (*1963) is Full Professor at TUM (Germany) since 2004 and Dean of the Faculty of Mechanical Engineering since 2016. His prestigious academic milestones include Stanford University, NASA Ames Research Center and ETH Zürich. He was speaker of the SFB TRR-40 and is Executive Editor of the Journal of Computational Physics. Prof. Adams is known for numerical modelling and experimental investigations with a focus on turbulence, multiphase flows, and microfluidics, and has contributed to aircraft and automotive aerodynamics. His academic impact manifests in more than 13,000 scientific citations and an h-index of 55.

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