BP 30: Focus Session: Controlling Microparticles and Biological Cells by Ultrasound (joint session BP/CPP/DY)

Recently ultrasound has emerged as a very promising physical modality to control the behavior of microparticles and even of biological cells, which can be moved and stimulated by sound waves. For biological cells, one can further control the effect of sound through gene expression (sonogenetics), similar to the control by light (optogenetics). However, because the wavelength of sound is much larger than the one of light, one of the challenges is to localize the effect of sound waves, e.g. by using gas bubbles. Here, we bring together experimental and theoretical researchers who currently explore the potential of ultrasound to control active and passive microsystems and to develop new applications ranging from biomedicine to soft robotics.

Organized by Peer Fischer and Ulrich S. Schwarz (Heidelberg)

Time: Thursday 10:15–12:45 Location: BAR/0106

Invited Talk BP 30.1 Thu 10:15 BAR/0106

Mechanogenetics for Cell ImmunoTherapy — •Yingxiao Wang — 1002 childs way, Los Angeles, CA 90089

Cell-based cancer immunotherapy is a promising therapeutic intervention for cancer treatment. However, non-specific toxicity against healthy tissues (e.g. off-tumor toxicity) is a major hurdle for solid tumor treatment. We have developed controllable on-switch gene cassettes in which a specific antigen production on the target cancer cell can be remotely and mechanically induced by an external focused ultrasound (FUS). FUS was applied to stimulate the production of the synthetic and clinically validated antigen on tumor cell surface orthogonal to the endogenous proteins. SynNotch was further engineered into primary human T cells (SynNotch-CAR T) to recognize the synthetic antigen expressed on the ultrasound-induced tumor cells and activate the production of CAR, which can lead to the recognition of a native tumor specific antigen (TSA) universally expressed on the whole population of tumor cells for immunotherapy. We applied this system to treat prostate cancer cells whose locally metastasized tumors are confined in space but intermingled with vessels and nerves. Our results showed that FUS can mechanically induce the synthetic antigen production in prostate cancer cells, which results in the engagement and activation of SynNotch CAR T cells for the tumor eradication. This local activation of engineered tumor cells by FUS should allow a high precision and safety in eradicating tumors. Hence, this approach for immunotherapy should open new opportunities to integrate engineering mechanics with genetic medicine for successful translation.

BP 30.2 Thu 10:45 BAR/0106

Shaping sound to tickle cells — •Dimitris Missirlis[1,2], Athanasios Athanassiadis[1,2], Rom Lerner[1,2], and Peer Fischer[1,2] — [1]Institute for Molecular Systems Engineering and Advanced Materials, Im Neuenheimer Feld 225, 69120 Heidelberg, Germany — [2]Max Planck Institute for Medical Research, Jahnstr. 29, 69120, Heidelberg, Germany

The ability to shape ultrasonic waves precisely is finding growing relevance in biomedical applications, where ultrasound is increasingly used to noninvasively stimulate biological tissues for therapeutic purposes. However, it remains an unsolved question how high-frequency ultrasound can interact with cells to excite biological responses. Our recent work on shaping and controlling ultrasound waves has provided us with a new tool to address the fundamental question how ultrasound interacts with and influences cells. To this end we have developed adaptable setups where we can control relevant ultrasound parameters in vitro as well as in vivo. By systematically examining the critical parameters, we discuss the role of different ultrasonic effects, including thermal effects, radiation forces, and sound-induced shear flows. Further, we discuss both physical and sonogenetic methods that can be used to enhance the coupling of ultrasound to cells.

BP 30.3 Thu 11:00 BAR/0106

A Theoretical Model for Ultrasound-Induced Intracellular Streaming — •Niels Gieseler[1,2,3], Falko Ziebert[1,2], and Ulrich S. Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University, Philosophenweg 19, Heidelberg 69120 Germany — [2]BioQuant, Heidelberg University, im Neuenheimer Feld 267, Heidelberg 69120 Germany — [3]Max Planck Institute for Medical Research, Jahnstrasse 29, Heidelberg 69120, Germany

Ultrasound is not only the basis of an essential imaging method for biomedicine, recently it has also become a promising avenue to control biological systems, for example, in sonogenetics or ultrasound neuromodulation. However, the underlying physical effects are not well understood, and a complete theoretical description is missing. In fact, many different physical effects compete, including radiation forces, streaming, cavitation, and local heating. Here, we focus on intracellular streaming, which might induce organelle movement or alter gene expression, as the steady second-order rotational flow generated by an acoustic source. As a model for the viscoelastic nature of cells and their surroundings, we use Oldroyd-B fluids. Building on existing work, we calculate the streaming flows inside and outside of a sphere sonicated with a plane wave. The streaming is treated as a second-order perturbation expansion of the Navier-Stokes equations, which is solved separately for both media and combined using suitable boundary conditions. Our work shows under which conditions intracellular streaming can be induced in biological cells.

15 min. break

Invited Talk BP 30.4 Thu 11:30 BAR/0106

Recent theoretical progress on sound-propelled microsystems — •Raphael Wittkowski — Department of Physics, RWTH Aachen University, 52074 Aachen, Germany — DWI – Leibniz Institute for Interactive Materials, 52074 Aachen, Germany

The research area of sound-propelled microsystems is growing fast and has a great potential for various future applications in engineering, medicine, and other fields. The progress in this area is accelerated by theoretical methods, as analytical modeling and computer simulations can provide new insights that cannot be obtained by experiments.

In this talk, I will address the theoretical investigation of sound-propelled microsystems and present examples from the recent research progress in this area. The talk will cover different types of sound-propelled microsystems including microrobots, micromachines, artificial muscles, and soft robots.

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BP 30.5 Thu 12:00 BAR/0106

Rarefaction wave amplification from non-resonant deforming bubbles — Yuzhe Fan, Saber Izak Ghasemian, and •Claus-Dieter Ohl — Otto-von-Guericke University, Magdeburg, Germany

Gas bubbles in liquids or soft matter exposed to acoustic waves behave as oscillators, with maximum response at their resonance frequency. When driven below resonance at sufficient pressure amplitudes, bubbles can collapse with strong energy focusing and even emit light; when driven near resonance, surface instabilities and fast jet flow develop during oscillation. Like other oscillators, bubbles cease to respond when driven far above resonance. Although their oscillations are minimal, bubbles in this regime act as pressure-release interfaces, can reflect high peak pressure shock into rarefaction wave, and may therefore seed cavitation when interacting with high-power therapeutic ultrasound. Yet, here we show that even diagnostic ultrasound with peak positive pressures as low as ∼10 MPa can nucleate cavitation in microseconds. This is caused through the non-resonant deformation of the bubble into a concave shape that refocuses scattered waves, amplifying the tension leading to microcavitation. Our findings reveal that cavitation can be triggered by high-frequency positive pressure over a much wider amplitude range than previously recognized, offering a new perspective for current safety guidelines for ultrasound bioeffects and applications in medical ultrasound.

BP 30.6 Thu 12:15 BAR/0106

Optimizing acoustically propelled microrobots using genetic algorithms — •Lennart Gevers[1,2,3] and Raphael Wittkowski[1,2,3] — [1]Department of Physics, RWTH Aachen University, Aachen, Germany — [2]DWI – Leibniz Institute for Interactive Materials, Aachen, Germany — [3]Institute of Theoretical Physics, Center for Soft Nanoscience, University of Münster, Münster, Germany

The promising potential applications of acoustically propelled microparticles demand methods to create particle designs that allow for targeted autonomous motion. Current methods remain largely based on experiments due to the intricate nature of the underlying dynamics. Large-scale computational studies, specifically when combined with optimization algorithms, are impeded by the cost of traditional acoustofluidic simulations.

In this talk, we present the implementation of an analytical framework describing non-Brownian motion of colloidal molecules driven by acoustic streaming. The analytical framework is combined with vectorized, GPU-accelerated, and distributed computation. This enables fast, large-scale simulations, where 10^5 trajectories over 10 s real time can be simulated on a normal personal computer within one minute. Coupling this approach with genetic algorithms reveals particle geometries, control parameters, and underlying principles for acoustically propelled particles that exhibit controllable and stable behavior over long times.

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BP 30.7 Thu 12:30 BAR/0106

Equations of motion for arbitrarily shaped acoustically propelled rigid microparticles — •Justus Schnermann[1,2,3] and Raphael Wittkowski[1,2,3] — [1]Department of Physics, RWTH Aachen University, Aachen, Germany — [2]DWI – Leibniz Institute for Interactive Materials, Aachen, Germany — [3]Institute of Theoretical Physics, Center for Soft Nanoscience, University of Münster, Münster, Germany

Much experimental research concerns the acoustic propulsion of microparticles, but theoretically, only axisymmetric particles with a stable orientation have been studied thus far. In this talk, we present an analytical derivation of the ordinary differential equation of motion for an arbitrarily shaped acoustically propelled rigid microparticle. This equation governs the time evolution of the orientation and position of the particle. Its parameters depend only on the particle's leading-order oscillation velocity field. Based on this equation, we classify qualitatively the possible long-term trajectories of arbitrary particles in unidirectional ultrasound.

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