Handy nanoquakes

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Electrically programmable Fourier-synthesized acoustic tweezers enable facile manipulation of micrometre-sized objects, colloids and living cells in a lab-on-chip device that combines high throughput with minimal invasive yet highly tunable force fields.

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Acoustic waves or phonons couple to literally any system, either classical or quantum. This unique property makes them extremely useful for a myriad of different, very interdisciplinary applications ranging from quantum technologies to the life sciences[1]. In the latter, precise control of fluids, particles and living cells[2,3] are important applications. However, to fully leverage the versatility of acoustic waves in these applications, the development of advanced control schemes is imperative[4].

It is well known that light and sound waves have many common properties. For instance, acoustic tweezers are the acoustic counterpart of optical tweezers[5], a technique by which microscopic objects can be trapped and moved by attractive or repulsive forces generated by focused laser light and the subject of the 2018 Nobel prize in physics. Similar to optical tweezers, in acoustic tweezers, a sound wave imprints a time- and position-dependent trapping field within a medium. For this purpose, sound waves can be elegantly excited on a piezoelectric chip in the form of a surface acoustic wave (SAW) that is generated by applying an alternating voltage to lithographically patterned interdigital transducers, as shown in Fig. 1.

Now, writing in *Nature Materials*, Shujie Yang and colleagues propose an acoustic tweezers approach that enables selective and reversible particle manipulation with high throughput and precision[6]. While the manipulation of the smallest amounts of liquids and colloids by SAWs has long been established, the grand challenge addressed by Yang and colleagues is in the creation of a universal platform for colloid and cell actuation with full programmability. The authors employ a harmonic acoustics approach for non-contact, dynamic, selective particle manipulation. This is achieved by harnessing the fact that SAWs can — as

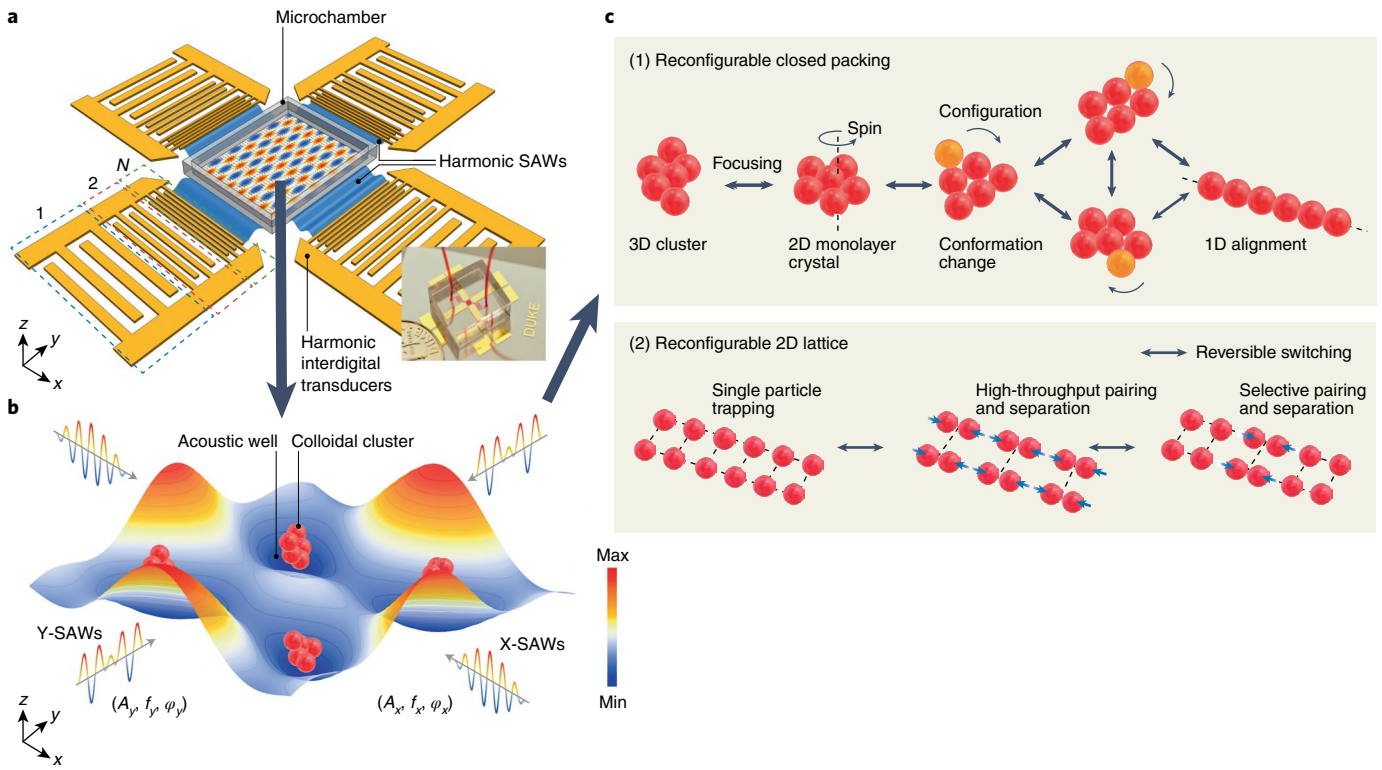

Fig. 1 | HANDS implements versatile acoustic manipulation of colloids in a lab-on-chip. a, SAW lab-on-chip layout for HANDS. **b**, Programmable acoustic potential. **c**, Colloid manipulation functionalities of HANDS. Figure reproduced with permission from ref. [6], Springer Nature Ltd.

any other wave — be superimposed to compose application-ready waveforms. This is achieved by Fourier synthesis of SAWs[7]. Like a music synthesizer or the audio card of a computer creates audible sound, a fundamental SAW of frequency f_1 and a discrete number of its harmonics $f_1 = N \times f_1$ are mixed with precisely set amplitudes A and phases φ (Fig. 1a,b). This way, trapping potentials for particles and cells are programmed on the surface of a chip. Setting the relative phases and amplitudes of different frequency components enables the precise and versatile single-particle manipulation shown in Yang and colleagues' work[6].

Specifically, the authors build on an established geometry of two overlapping perpendicular SAW fields shown in Fig. 1a. Combining this geometry with freely programmable SAW waveforms, they demonstrate the generation of arbitrary patterns for precise and selective manipulation of colloids and cells. The synthesized waveforms create trapping potentials with programmable spacing and shape (Fig. 1b), which opens a wide range of parameters and enables diverse applications. An important feature of the harmonic SAW platform proposed by Yang and colleagues is that it comprises several functionalities on a single platform — an essential requirement for on-chip actuation and sensing.

The method reaches remarkable levels of control beyond single particle trapping shown in Fig. 1c. For example, after capturing a well-defined number of micrometre-size objects, such as microparticles or cells, these objects can be clustered and arranged in different configurations within individual traps. The shaped acoustic waveforms can even create spinning motions of colloidal crystals or arrange them into long, one-dimensional strings.

Yang and colleagues also demonstrate the high throughput of their approach, as exemplified impressively in experiments on reversible single-colloid pairing and separation, where they show that more than 100 pairs can be studied simultaneously. This parallel sampling dramatically reduces the number of experiments necessary to obtain reliable statistics. This paves the way to swift, time-efficient analyses, important for rapid diagnostics and comprehensive statistics. The massively parallel nature of the underlying acoustic tweezer approach stands out compared with other established and commonly applied techniques to study intercellular adhesion, such as atomic force microscopy, micropipette aspiration or single optical tweezers.

Yang and co-workers take advantage of the remarkable level of tuneability enabled by their technique and implement a full set of methods to measure intercellular adhesion processes and quantify key parameters of cell adhesion using various cell lines. The authors demonstrate, on the one hand, the ability to quantify different expression levels of cell adhesion molecules. On the other hand, they also prove the sensitivity of the approach towards changes in the cytoskeleton of the cell. The demonstrated reversible cell–cell pairing for the quantification of intercellular adhesion forces and lifetimes is impressive, opening up possibilities for a wide field of biophysical and cell biology applications. For instance, the effect of membrane proteases regulating the hypoglycosylation of membrane proteins could finally be fully unravelled. Another long-envisioned goal is the assembly of artificial organs or neural networks from their individual constituents using SAWs[8]. For this purpose, the scale of the acoustic traps has to be flexibly matched to different types of cells involved. Also, intracell stimulation may become possible by adding short-wavelength harmonics. Having demonstrated the power of the harmonic acoustics for dynamic and selective (HANDS) platform, the techniques can

be matured and advanced to unexpensive, easy-to-use tools for non-experts in acoustics to tackle key challenges at the forefront of cell biology, colloidal systems or biological physics.

Coming back to the universal nature of acoustic nanotechnologies[1], the work by Yang and co-workers[6] may have cross-disciplinary influence going beyond the parallelized set of acoustic tweezers. The induced spinning motion of colloids may prove very useful to study and harness fundamental properties of SAWs, such as their acoustic spin[9]. Indeed, concepts exist even to create acoustic lattices in quantum technologies[10]. SAW-based quantum devices typically require a substantial increase of the different frequency components to the gigahertz domain. The corresponding small feature size poses a challenge to nanofabrication that could be alleviated by introducing novel 'fast' SAW substrate materials supporting higher SAW velocities. Furthermore, superconducting electrode materials may prove viable to reduce ohmic losses and resulting unwanted heating to preserve the coherence quantum states. The now demonstrated level of control marks a big leap towards a SAW-programmable brain-on-chip, or even a SAW-based quantum simulator. ❐

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Competing interests

The authors declare no competing interests.