

Concept Paper

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Concept Paper

Towards Enabling Diatom Frustule Integration in Advanced Micro/Nanosystems: Automated Micromanipulation as a Promising Approach

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Abstract

Diatoms—unicellular microalgae essential for global ecosystems—synthesize nanostructured siliceous frustules composed of valves and girdle bands. In recent years, these frustule components have attracted increasing attention as sustainable, eco-friendly, and cost-effective alternatives to selected artificially fabricated micro/nanostructures used in micro- and nanosystems, particularly in fields such as photonics, sensing, and microfluidics, leading to the rise of diatom nanotechnology. Yet, the fabrication of commercially viable diatom-based devices remains hindered by several bottlenecks, including challenges associated with the precise assembly and integration of frustule-derived components within sophisticated micro- and nanosystems. In this perspective, we focus on these challenges and propose automated micromanipulation as a potentially transformative approach for addressing them.

Keywords: diatom frustule; automated micromanipulation; microsystems; microfluidics; photonics

Diatoms: A Sustainable Source of Nanostructured Siliceous Frustules

Diatoms are a major group of microalgae that play crucial roles in the global ecosystem, as they generate at least 20% of the global atmospheric oxygen and about 40% of organic carbon in the oceans [1–5]. They are a very ecologically successful group, as evidenced by their abundance in many aquatic habitats, their wide global distribution, and their remarkable diversity [6,7]. Through elegant biomineralization processes, diatoms synthesize a unique nanostructured cell wall—known as frustule—composed of amorphous hydrated silica [3,8]. The geometry and ultrastructure of frustules vary greatly among species and genera [3,9], as illustrated in Figure 1. Each frustule—regardless of its geometry—consists of two overlapping valves and one or more girdle bands [10]. These siliceous parts are often highly ornamented and porous, with pore sizes ranging from a few nm to a few μm [10].

Several diatom species have been successfully isolated and cultivated on laboratory and pilot scales for various purposes, whereas large-scale commercial cultivation remains limited [11,12]. Biomass obtained from cultivation can be used to extract high-value metabolites, including pigments and lipids [13–15], while the valves/girdle bands can be retrieved from the biomass by oxidation of organic materials to be utilized in applications [16]. It should be noted that diatom siliceous components can also be extracted from natural sedimentary rocks called diatomite, which contain fossil diatom frustules [17,18]. For several decades, diatomite has been widely used in various applications, such as filtration, insulation, building materials, abrasives, and as functional additives and fillers, owing to their unique physical and chemical properties [19–21]. Although fossil frustules

are inexpensive and readily available in large quantities in the market, sourcing frustules from cultivation offers sustainability and enables better control over their structural and functional characteristics, which is highly required for advanced technological applications [19].

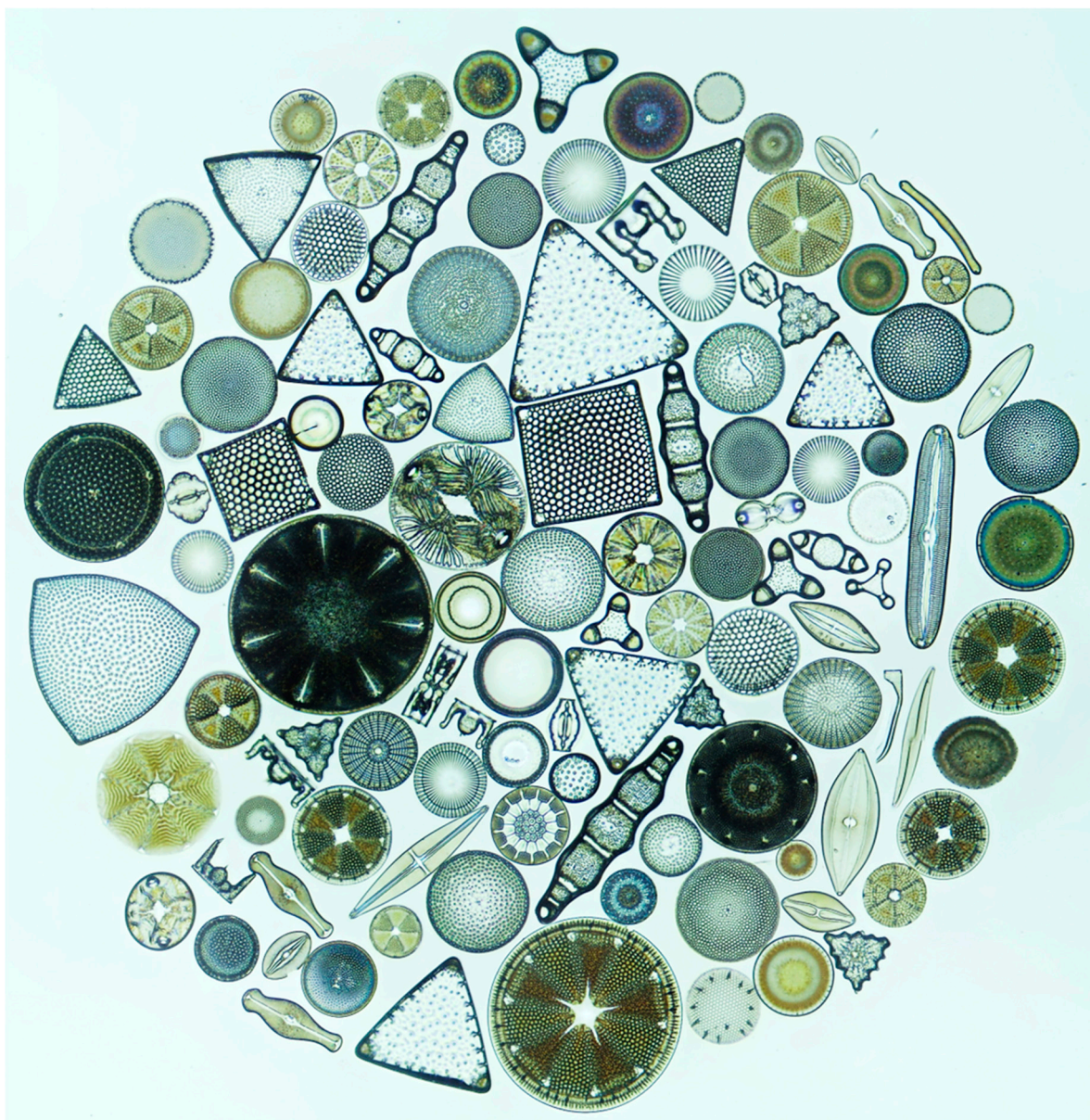


Figure 1. An LM micrograph showing cleaned diatom valves arranged and fixed on a glass substrate, prepared and imaged by Emiliano Bellotti. This micrograph reflects precise control over position, spacing, and orientation of diatom valves, achieved through manual micromanipulation.

The Rise of Diatom Nanotechnology

At the end of the 20th century, the idea of utilizing diatom frustules in nanotechnology applications was proposed, taking advantage of their intrinsic nanoscale structural features [22]. This approach is promising as diatoms typically build their frustules with high reproducibility and nanoscale precision that challenges artificial nanofabrication techniques, while relying only on basic nutrients (including silicic acid), sunlight, and carbon dioxide under ambient conditions (see, *e.g.*, [23]). These ideas gained attention among several researchers from various science and engineering disciplines. In 2003, the term 'Diatom Nanotechnology' was introduced [8]. In the same year, several researchers interested in this emerging field met at the Diatom Nanotechnology Workshop, held as part of the 17th North American Diatom Society meeting, to foster collaborations and exchange ideas

[24]. Since then, the number of relevant publications has increased dramatically, associated with increasing applications in fields such as drug delivery, microfluidics, sensing, catalysis, photonics, and energy harvesting [25]. However, several key bottlenecks still hinder the transfer of these advanced applications from the laboratory to the market, such as scaling up cultivation and silica extraction processes for species intended for nanotechnology applications. Additionally, for fabricating diatom-based photonic and microfluidic devices, the precise assembly and integration of frustule-derived components within these sophisticated micro/nanosystems remains challenging, especially to obtain commercially functioning devices.

Establishing a Monolayer of Diatom Valves

Achieving a uniform monolayer of diatom valves over large substrate areas is considered among the key challenges for integrating these valves into certain optoelectronic devices, such as solar cells, where valves act as photonic crystal-like structures that improve the device efficiency [26–28]. Conventional techniques, such as drop-casting and spin-coating, have been investigated and can produce relatively uniform films when optimized [26,28]; however, achieving consistent coverage across large substrate areas remains challenging. Other techniques, including floating, droplet-based, and bubble-assisted assembly, have been reported in the literature to enable better control over monolayer formation and to influence valve orientation [29–31].

Beyond uniformity, achieving strong adhesion of the diatom monolayer on substrates is essential for device stability. Various strategies have been reported in the literature to enhance adhesion, including thermal annealing [32], promoting chemical bonding between the diatom valves and the substrate (*e.g.*, HF-assisted bonding method [33]), and surface modification of the substrate using polyelectrolyte multilayers [34].

Microscale Assembly and Immobilization of Diatom Valves

In some applications, such as the fabrication of diatom-based highly sensitive and selective biosensing platforms [35], a continuous monolayer does not provide the required functionality. Instead, a controlled spatial distribution of diatom valves at the microscale is needed. Wang *et al.* [36] demonstrated a patterning strategy based on inkjet printing combined with multilayer polyelectrolyte deposition (prepared layer-by-layer). In this approach, a negatively charged top layer was established over the substrate, followed by selective deposition of a positively charged polyelectrolyte via inkjet printing, enabling electrostatic binding of negatively charged diatom valves onto predefined patterned regions (with feature sizes of approximately 300–350 μm). Another patterning strategy was reported by Wang *et al.* [37], where photolithography was used to define microscale patterns on a substrate, followed by ultraviolet-assisted formation of covalent Si–O–Si bonds between diatom silica and a PDMS substrate. This enabled selective and stable immobilization of diatom valves within predefined regions.

Single-Valve Manipulation and Positioning

In applications requiring the use of individual diatom valves, such as their integration as functional microelements into microfluidic systems and photonic devices, precise control over their positioning, spacing, and orientation is critical. Well-established micro- and nanoscale manipulation techniques, such as optical tweezers, are widely applied to a broad range of microparticles [38]. These techniques generally rely on predictable particle responses to externally applied fields, which in turn depend on relatively uniform geometry, density, surface charge, and optical or mechanical properties. Their direct application to diatom valves, however, remains challenging due to the inherent heterogeneity of valves, which often exhibit complex three-dimensional geometries and considerable variability in size and shape among species.

Manual Micromanipulation

In previous studies, manual micromanipulation has emerged as a practical approach for achieving precise control over both the position and orientation of individual diatom valves (see, for example, Losic *et al.* [39] and Wang *et al.* [40]). This approach has also been adopted by diatom hobbyists and artists to arrange diatom valves into intricate patterns and designs [41], as shown in Figure 1. This technique typically relies on microneedles mounted on micromanipulators, in combination with optical microscopy, to enable micrometer-scale positioning accuracy (*e.g.*, Figure 2). Using such a system, individual valves can be picked up and precisely transferred to specific locations on substrates, although the process may be influenced by surface forces and environmental conditions. Despite offering exceptional control over position and orientation, this method remains inherently low-throughput, operator-dependent, and difficult to scale. These limitations highlight the need for automation.

Automated Micromanipulation

To overcome the limitations of manual micromanipulation, the development of an automated system for handling individual diatom valves is proposed, as outlined in Figure 3. A feasible automated micromanipulation platform would integrate at least three main components: (i) an imaging and recognition system, (ii) a decision-making and control system, and (iii) a micromanipulation unit.

The imaging and recognition system would combine high-resolution optical microscopy with deep learning-based image analysis, particularly convolutional neural networks (CNNs) trained on carefully selected image datasets [42,43], to enable accurate identification and classification of diatom valves within complex samples containing debris and broken fragments. Several studies have investigated CNN-based approaches for diatom valve identification and classification in the context of taxonomy and forensic applications (*e.g.*, [44–47]), providing a strong foundation for developing the proposed system. Beyond identification, the system may also be adapted to support the extraction of key structural features such as symmetry, pore structure, and assess valve orientation, thereby providing information to support downstream decision-making processes.

Moreover, the decision-making and control system would translate visual information into actionable manipulation commands. This includes identifying and selecting suitable intact valves for pick-up, determining optimal placement locations, and defining the desired orientation based on device-specific requirements. This could be implemented using a combination of rule-based algorithms and adaptive learning strategies [48], enabling real-time feedback and dynamic adjustment during manipulation.

Furthermore, the physical manipulation could be performed using microrobotic tools such as microgrippers, microneedles, or vacuum-based probes. These tools must be carefully designed to handle the fragile and geometrically complex diatom valves, while minimizing damage and ensuring precise placement. Integration with high-precision positioning stages and closed-loop feedback systems would be essential to achieve reliable operation at the microscale.

However, it should be noted that the realization of a fully automated platform for diatom valve manipulation remains technically challenging despite recent advances in micromanipulation and automation. The variability in diatom valve geometry, size, and surface properties complicates both recognition and manipulation processes. Additionally, microscale forces—such as van der Waals interactions and capillary effects—can significantly influence pick-up and release behavior. The fragility of siliceous structures of some species further demands precise control of applied forces and environmental conditions. These challenges, however, are not prohibitive and could be addressed through interdisciplinary approaches integrating microrobotics, materials science, and artificial intelligence.

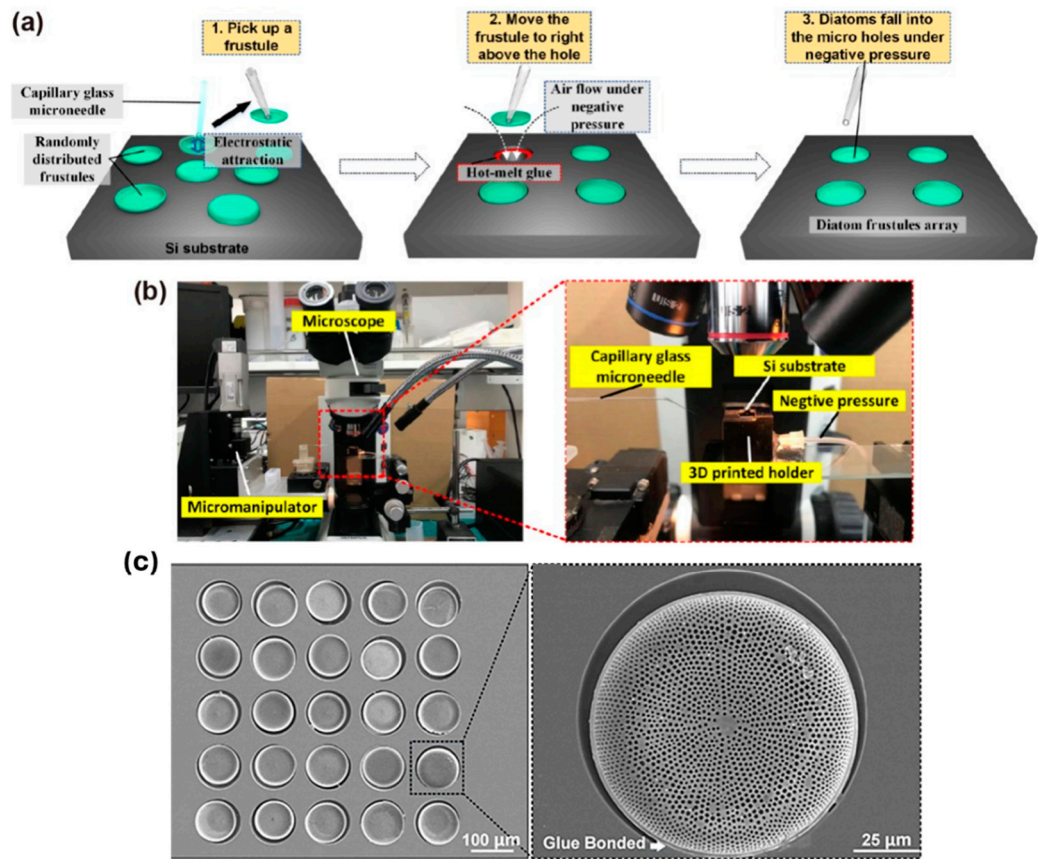


Figure 2. Example for manual micromanipulation from Wang *et al.* [40]. (a) Schematic diagram illustrating the micromanipulation steps followed in this study. (b) Images of the micromanipulation setup. (c) SEM image of the fabricated microarray of *Coscinodiscus* sp. These images were modified and combined from the supplementary materials of Wang *et al.* [40] and are reproduced here under the Creative Commons Attribution 4.0 License.

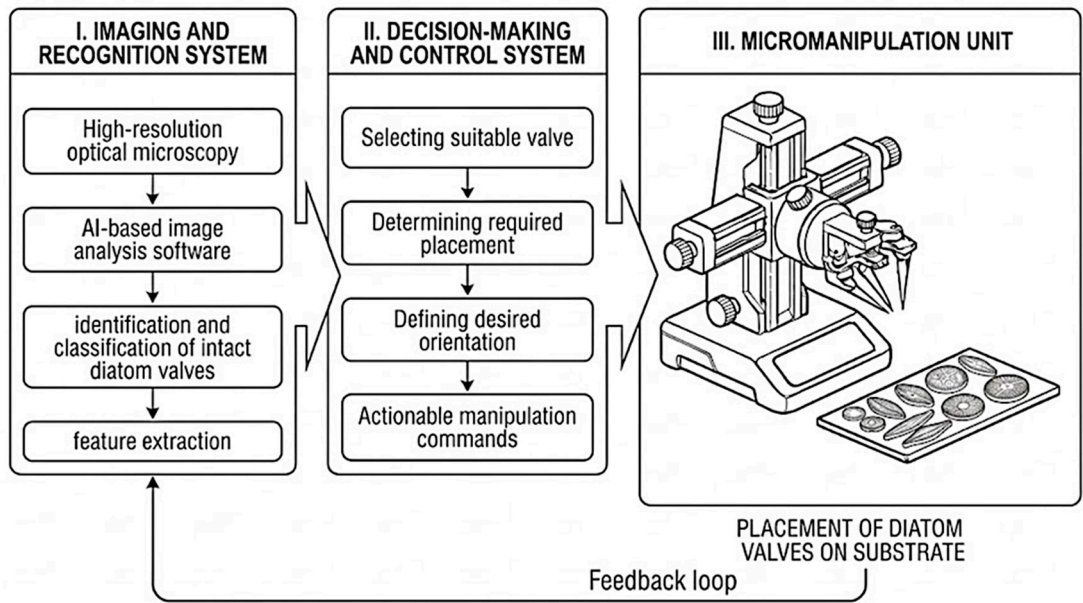


Figure 3. An outline of the proposed automated micromanipulation system.

Conclusion and Outlook

Diatom frustules are a remarkable class of naturally engineered micro- and nanostructures, offering a sustainable and highly versatile platform for a broad range of applications. Over recent years, diatom nanotechnology has demonstrated successful implementation in many fields at laboratory scale. Yet, several obstacles limit the translation of diatom-based technologies from lab to market. In this perspective, we propose an integrated automated micromanipulation system for single-valve handling, positioning, and assembly as a central enabling strategy for diatom-based device fabrication. Such automated platform could significantly advance the field by enabling the transition from proof-of-concept demonstrations toward scalable and reproducible fabrication of diatom-based devices. This approach could unlock the potential of diatom frustules as building blocks for next-generation micro- and nanosystems.

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