# Self-Propelled Nanotools Drilling into Cells and Tissues

Samuel SANCHEZ; Wang XI, Alexander SOLOVEV, Oliver SCHMIDT

*Institute for Integrative Nanosciences, IFW Dresden, Helmholtzstr. 20, D-01069 Dresden, Germany*
*s.sanchez@ifw-dresden.de*

***Abstract* — We designed nanoscale tools in the form of autonomous and remotely guided catalytically and magnetically self-propelled micro- and nanotools. Asymmetrically rolled-up nanotools move in a corkscrew-like trajectory, allowing these tiny tubes to drill and embed themselves into biomaterials (fixed HeLa cells and tissues). First, we designed the smallest self-propelled nanojet engine (InGaAs/GaAs/(Cr)Pt) with diameters in the range of 280–600 nm, which move in hydrogen peroxide solutions with speeds as high as 180 µm.s$^{-1}$ and perform advanced tasks such as drilling into cancer cells. Also, we demonstrated that tubular fuel-free Ti/Cr/Fe micro-drillers containing sharp tips can be applied for mechanical drilling operations of porcine liver tissue *ex vivo*. An external rotational magnetic field is used to remotely locate and actuate the micro-drillers in a solution with a viscosity comparable to that of biological fluids (e.g., blood).**

***Index Terms* — Drilling, nanotools, nanojet engine, remotely controlled, rolled-up nanotechnology.**

## I. INTRODUCTION

The mimicry of mechanized macroscale functions at the nanoscale is important for nanomanufacturing and nanorobotics. However, even simple macroscopic tasks are extremely challenging at these small size scales, since it is hard to achieve and control nanoscale actuation reproducibly, reversibly and especially in a wireless manner.

The creation and implementation of dynamic micro- and nanoscale mechanized structures with advances in micro/nanotechnology are believed to revolutionize minimally invasive surgery (MIS). The first step towards enabling this vision is to create small tools that can mimic the functionality of larger tools utilized in surgery [1]. In addition, it is necessary to develop methods so that these tools can be guided and implemented in a tether-free manner. One class of tools in surgery is the sharp surgical instruments that are widely utilized for making incisions. Some of these surgical instruments are enabled by electromagnetic motors on the macroscale, but it can be very challenging to harness the energy in a tether-free manner required to perform drilling at smaller size scales.

One approach to power micro- and nanoscale tools involves the catalytic conversion of chemical energy (energy-rich molecules in solution) into mechanical energy [2]. Catalytically constituted micro- and nano-structures can accelerate the decomposition of hydrogen peroxide and enable the self-propulsion of micro- and nanomotors, pumping of fluids, and transport of colloidal particles and cells [2d-f].

Such miniaturized and remote-controlled microtools may have high potential for in vivo applications in the near future in the circulatory, the urinary and the central nervous systems [3]. However, to fabricate cost-effective and operative MIS devices, scientists need to make use of fabrication techniques that enable mass production of non-trivially shaped three dimensional structures, often with multiple classes of materials [4]. In this context, rolled-up nanotechnology –previously envisioned for nanodriller applications [5]– meets the above described requirements.

## II. RESULTS AND DISCUSSION

We fabricated catalytic tubes with diameters in the sub-micrometer range and investigated control over their catalytic motion. By using molecular beam epitaxy (MBE), thin films of InGaAs/GaAs were deposited on sacrificial AlAs layers and bulk GaAs substrate, and a thin catalytic Pt film sputtered on top. By rolling up those nanomembranes, we fabricated catalytic nanotubes with diameters approximately 20 times smaller than previously reported rolled-up microjets [6] and half the size of the recently designed nanojets (Figure 1) [7]. Consequently, we reported the smallest man-made catalytic jet engines.

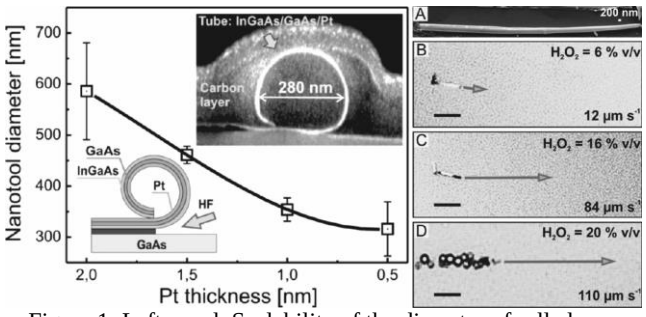


Figure 1: Left panel. Scalability of the diameter of rolled-up nanotubes consisting of hybrid heteroepitaxial catalytic InGaAs (3 nm)/GaAs (3 nm)/Pt thin films. Bottom inset shows the rolled up fabrication process by selective underetching of the sacrificial AlAs (20 nm) layer. Top inset depicts a SEM image containing a focused-ion-beam (FIB) cut of an individual tube composed of InGaAs/GaAs/Pt (0.5 nm). Right panels: A) SEM image of an InGaAs/GaAs/Cr/Pt (3/3/1/1 nm) nanotube with average diameter 600 nm. B-D) Motion and speed of cylindrical catalytic rolled-up nanotubes (nanojets) in different concentrations of fuel solution. Scale bar in (B) and (C) is 15 µm and in (D) is 30 µm.

The catalytic nanojets are powered by the decomposition of $H_2O_2$ into molecular oxygen which accumulates in the small cavity and eventually gets

released from one end of the nanotube as visible bubbles (Figures 1). Figures 1 illustrate the motion and trajectories of InGaAs/GaAs/Cr/Pt (3/3/1/1 nm) nanojets immersed in different concentrations of peroxide fuel. These results demonstrate that bubble driven catalytic nanojets can indeed overcome Brownian diffusion as well as the high viscous forces of the fluid at low Reynolds numbers. Many of the fabricated nanotubes present a sharp tip clearly seen in Figure 2C and Figure 3A (b-c). The release of bubbles from these rolled-up structures is asymmetric in nature, thus the catalytic nanojets move either in curved trajectories (Figure 1B, C and D) or in a corkscrew fashion (Figure 2A).

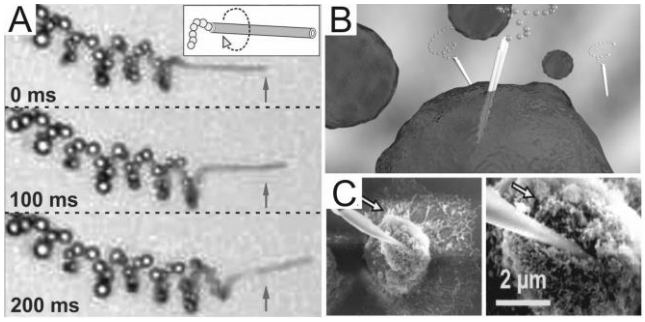


Figure 2. (A) Corkscrew-like motion of a rolled-up microjet. Schematic (B) and SEM images (C) of a rolled-up microjet embedded into cells.

We exploited the corkscrew propulsion (Figure 2A) of the nanojets to drill into biomaterials such as those constituting Hela cells, which are an immortal cell line derived from cervical cancer. It should be noted that we utilized paraformaldehyde to fix the cells prior to the drilling experiments for two reasons; (a) we wanted to remove the influence of any chemically induced deformation of the cell during drilling in the $H_2O_2$ fuel, (b) These fixed cells represent a cross-linked version of a realistic cellular biomaterial, so we rationalized that if the nanotools could generate enough force to drill into fixed cells, they would likely have more than enough force to drill into un-cross-linked cells. The type of motion needed for drilling is clearly shown in Figure 2 by optical microscope sequences of an individual nanojet which self-propels in a screw-like motion during 200 ms at a rotational frequency of 10 Hz (fuel composition: 20 % v/v $H_2O_2$, 10 % v/v surfactant). Straight arrows in the images indicate the linear displacement of the nanojet during the studied time. The inset of Figure 2A depicts a schematic of the rotation of the nanojet during translation. The schematic image in Figure 2B displays nanotools which self-propel and embeds itself into a fixed Hela cells. Once the cellular boundary is reached, the nanotools stick to it and start drilling into the cellular biomaterial over several minutes (Figure 2C).

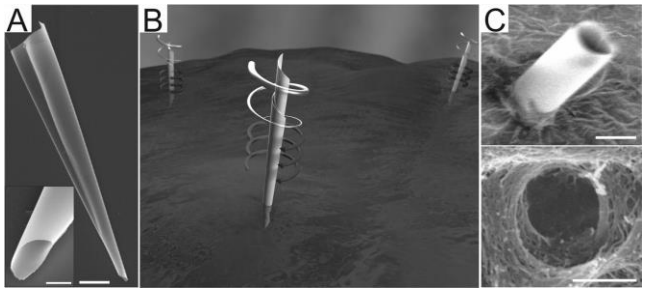


**Figure 3.** Magnetic microdrillers. A) SEM images of a sharp microtube. B) Schematic of the motion and drilling of microtubes into tissues *ex-vivo* using rotating magnetic field. C) **(upper panel)** SEM image of a microdriller embedded into the pig liver section after drilling; **(lower panel)** SEM image showing the drilled hole in the pig liver section after extracting the microdriller by a strong permanent magnet (500 mT). Scale bar: 1µm in (A), 5µm in (B) and (C).

Although the fuel employed for self-propulsion is still toxic to sustain viable mammalian cellular functions, alternative mechanisms of powered motion and working conditions foresee the use of this concept in diverse applications such as biomedical engineering, biosensing and biophysics. While hydrogen peroxide may be acceptable for applications in nanomanufacturing and nanorobotics, biocompatible fuels need to be developed for live-cell applications. Nonetheless, due to the reduced dimensions but yet the high propulsion power, our results suggest strategies of using shape, size and asymmetry of catalytic nanostructures as tools to realize mechanized functions at the nanoscale.

To circumvent the limited applications of toxic fuel in vivo, an attractive approach relies on the fabrication of "fuel-free", e.g. those powered by external magnetic fields. Recently, the enzymatically-triggered and tetherless thermobiochemical actuation of miniaturized grippers and tools, magnetically guided into liver tissues, was demonstrated.[1a,b]

With the same rolled-up technology, we fabricated tubular Ti/Cr/Fe micro-drillers containing sharp tips (Figure 3A) that can be applied for mechanical drilling operations of porcine liver tissue ex vivo (Figure 3B). An external rotational magnetic field is used to remotely locate and actuate the micro-drillers in a solution with a viscosity comparable to that of biological fluids (e.g., blood). Changes in the frequency of the rotating magnetic field results in the switching of the rotational orientation of the micro-driller from a horizontal to a vertical one, which lifts the tubes and makes them suitable for drilling purposes. When microtools are place on hard planar surfaces (e.g. glass or silicon) and re-orient to the upright rotation, they are able to "walk" towards the center of the rotational magnetic field.

To demonstrate the drilling operation (Figure 3B), a pig liver section was placed at the centre of the magnetic field in a petri dish containing microtools in the working solution (soap-water, 50 % (v/v)). The angular frequency was increased to 1150 rpm at which the microtools switched their orientation from horizontal into vertical

one. Thereafter, the microtools were guided to the desired locations and start the drilling operation from tens of minutes to few hours. It was observed that the microtools retain upright orientation and the initial rotation frequency (~1150 rpm) immediately after reaching the tissue, but significantly slowed down in rotation frequency to few hundreds rpm (~400 rpm) after several minutes standing on the tissue. However, that is not the case for microtools rotating on rigid glass surface, where they rotate at frequencies similar to the applied external rotation field (~1150 rpm).

Using these micro-drillers, we show that magnetic rolled-up microtubes can be used for directed drilling holes in soft matter using porcine liver tissue as a model system.

## III. CONCLUSION

We demonstrated the fabrication of 3D ferromagnetic microdrillers with sharp tips for drilling operation of soft biomaterials. The rolled–up microtools were formed from 2D nanomembranes of trapezia geometry. It is possible to dynamically switch the orientation of the microtool from a horizontal to a vertical position by changing the frequency of the external processing magnetic field and the viscosity of the solution. We presented magnetic control, drilling and guidance of fuel free microtools toward tissue samples ex-vivo. We also demonstrated that such incision can be performed in a fluid with viscosity similar to blood, which is ideal for future use in the field of microrobotics for minimally invasive surgery. The surface friction between the sharp ends and the tissue is believed to facilitate the drilling operation. The advantage of the tubular structure of the microtools is that the hollow structure might be utilized in the future for filling up with drug carrying gels for site directed drill and delivery systems, e.g., cholesterol degrading enzymes for clearing the arterial blockages and plaque removal nanorobots for minimal invasive surgery.

## ACKNOWLEDGMENTS

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