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ABSTRACT
Free liquid jets are a common sample delivery method in serial femtosecond x-ray (SFX) crystallography. Gas dynamic virtual nozzles (GDVNs) use an outer gas stream to focus a liquid jet down to a few micrometers in diameter. Such nozzles can be fabricated through various methods (capillary grinding, soft lithography, digital light processing, and two-photon polymerization) and materials, such as glass, polydimethylsiloxane, and photosensitive polyacrylates. Here, we present a broadly accessible, rapid prototyping laser ablation approach to micromachine solvent-resistant and inert Kapton polyimide foils with highly reproducible geometric features that result in 3D flow-focused GDVNs suitable for crystallography experiments at synchrotrons and free-electron laser facilities.

INTRODUCTION

Liquid jets are freely flowing liquid columns that achieve reliable sample delivery with minimal scattering background and a high signal-to-noise ratio. Many samples, in particular biological ones, quickly degrade upon x-ray exposure due to the high radiation dose absorbed and, hence, need to be constantly replenished. Accordingly, liquid jet-based sample delivery achieves this and has become well established in x-ray scattering and diffraction experiments that require multiple exposures for completing a single dataset, such as SAXS (small-angle x-ray scattering),1,2 WAXS (wide-angle x-ray scattering),3,4 and SFX (serial femtosecond x-ray) crystallography.5,7

A major advance in the fabrication of liquid jet devices was the development of the gas dynamic virtual nozzle (GDVN) by DePonte et al.6 that is based on the flow-focusing formulations by Gañán-Calvo.9 In their GDVN design, the orifice in a flat plate used by Gañán-Calvo was replaced with an aerodynamically converging sidewall inside a 1-mm-diameter glass capillary for coaxial gas-focusing. The co-flow of the sheathing gas constitutes a virtual nozzle for the liquid to flow through. Here, the combined forces, involving tangential shear and extensional stress, viscous stress, and...
surface tension, lead to the acceleration and convergence of the liquid without wall contact. This converging fluid meniscus results in a cylindrical microjet with diameters down to a few micrometers and below or it can be tuned to break up into fine sprays upon gas flow adjustment. The reduction of jet diameter allows for stable jetting at very low liquid flow rates on the order of a few hundred μl h⁻¹, which in turn reduces the sample consumption. Furthermore, low flow rates allow the operation of thin jets, which can reach velocities suitable for x-ray pulses with MHz repetition rates.

First, DePonte et al. reported glass-based GDVNs. Later, Calvey et al. improved the nozzle geometries and applied the injectors in x-ray free-electron laser (XFEL) experiments. However, a major drawback for glass nozzles is their highly manual fabrication that renders production scale-up difficult and often yields poor device reproducibility. Trebbin et al. introduced soft lithography-based GDVNs constructed from poly(dimethylsiloxane) and compatible with high-throughput, cost-efficient, and highly reproducible fabrication, while allowing for more design variations. Along this rationale, stereolithography was used to 3D print high-resolution nozzles from photocured polymers, which has recently led to highly compact nozzles and micromixers. Both these approaches result in devices with a lower solvent resistance than the original glass-based GDVNs. A method to micro-machine GDVNs from inert materials would thus be highly desirable for applications that require a wide organic solvent compatibility.

The results presented here describe the adoption of the geometric design for the photolithographically structured master template (reported by Trebbin and co-workers for the PDMS devices) into the trajectory of a pulsed UV laser beam to fabricate all polyimide GDVNs, capable of generating stable microjets at high pressures. Pulsed UV laser micromachining of Kapton polyimide sheets, in conjunction with melt-processible fluorinated ethylene propylene (FEP) foils, resulted in chemically inert, but also x-ray transparent GDVNs. The foils were first rinsed with isopropanol followed by water and dried in an oven at 75 °C before use. The foils were fixed to a small metal plate and mounted on the x–y stage of the laser micromachining system. The laser beam trajectory was controlled using the software Process Power (OPTEC, ver. 1.0) based on a DWG file (created with AutoCAD 2017), which resulted in the final channel geometry. Following a similar approach described by Barrett et al., the depth of the microchannel was controlled by the number of pulses per spot (11 mJ/pulse) to define the custom 3D structure. Within the computer-aided design (CAD) file, the designated color for a given line represents a mask through which the laser beam passes, defining its size and shape and determining the final channel widths structured onto the sample. Different layers of lines were then used to assign different pulse frequencies and numbers of shots per spot (e.g., layer 1 represents 1000 shots to write through the entire Kapton) to enable custom depths of the ablated material. For a fast writing speed, the pulse frequency was set at 200 Hz. The nozzle design is provided as a supplementary material file in the DWG format.

In general, the microstructuring followed a two-step procedure (Table I provides a detailed description of the utilized design parameters). First, the channels were written as a sequence of polylines onto the flat substrate as shown in Figs. 1(a)–1(c). Then, the foil was flipped 90° to access the 125-μm-thick Kapton edge face-on [Fig. 1(d)]. In this manner, the main channel (MC) was connected via circular orifices with the gas-focusing region. Various widths for the microchannels were chosen to mimic the geometry of the photolithography photomask previously used for PDMS-based nozzles. For the MC (liquid flow), a circular-shaped beam with a diameter of 30 μm was chosen. The square bracket-shaped gas-focusing region was comprised of a 125 μm deep (i.e., all Kapton ablated) mixing area and a 12 μm wide circular orifice (referred to as “A,” generated by 1800 shots at 50 Hz) in perpendicular orientation connected to the main channel. The outer circular orifice of the nozzle (“B”), which

**Experimental**

**Chemicals and materials**

Acetone and isopropanol were purchased from Roth, Kapton® HN foils (125 μm thickness) from Detakta, and Teflon®-coated Kapton FN (FF16140) (50 μm thickness) from Müller Ahlhorn. PEEK tubings with an outer diameter (OD) of 1/16″ = 1.59 mm and an inner diameter (ID) of 0.025″ = 635 μm were purchased from Scientific Commodities, PEEK fittings containing 1/16″ inner diameter (ID) of 0.025" and a cross-sectional diameter of 1.02 mm were purchased from COG.
| Parameter | Definition | Dimension (μm) | Index color for mask (R/G/B values) | Layer |
|-----------|------------|----------------|------------------------------------|-------|
| \(w_{MC1}\) | Width of the main channel at nozzle region (liquid inlet) | 30 | 11 (255/127/127) | 1 |
| \(w_{SC1}\) | Width of the side channel at nozzle region (gas inlet) | 30 | 11 (255/127/127) | 0 |
| \(w_G\) | Width of the gas-focusing region | 30 | 11 (255/127/127) | 1 |
| \(\alpha\) | Angle of the side channel (24°) | 30 | 11 (255/127/127) | 0 |
| \(L_A\) | Length of the gap between main channel and gas-focusing region (orifice length of A) | 60 | 11 (255/127/127) | 1 |
| \(d_A\) | Diameter of inner orifice | 12, 30 | 7 (255/255/255), 11 (255/127/127) | 0 |
| \(L_B\) | Length of the gap between gas-focusing region and nozzle exit (orifice length of B) | 65 | 11 (255/127/127), 14 (127/0/0) | 1 |
| \(d_B\) | Outer orifice diameter | 30, 65 | 11 (255/127/127), 14 (127/0/0) | 1 |
| \(L_{G-B}\) | Distance from inner orifice outlet to outer orifice outlet | 95 | 11 (255/127/127), 14 (127/0/0) | 1 |
| \(L_{A-B}\) | Distance from main channel inlet to nozzle outlet | 155 | 11 (255/127/127), 14 (127/0/0) | 1 |
| \(L_E\) | Diameter of laser for cutting the nozzle edge | 50 | 13 (165/82/82) | 1 |
| \(w_{MC2}\) | Width of the main channel (liquid inlet) | 50 | 13 (165/82/82) | 1 |
| \(w_{MC3}\) | Width of the main channel (liquid inlet) | 85 | 15 (127/63/63) | 1 |
| \(w_{SC2}\) | Width of the side channel (gas inlet) | 150 | 18 (38/0/0) | 1 |

**FIG. 1.** ([a] and [b]) Computer-aided design (CAD) with the trajectories for the UV laser beam (orange). The blue lines represent the geometry of the PDMS nozzle (photomask design for lithography-based GDVN as described in Trebbin et al.), which served as a template for the microchannels in Kapton. The green circles visualize the selected size of the laser beam, and the magenta circles depict the inner diameter of the FKM O-rings of the nozzle holder. ([c] and [d]) Photographs of the final laser-written Kapton foil in top and face-on view with an inner orifice diameter \((d_A)\) of 12 μm and an outer orifice diameter \((d_B)\) of 30 μm. Denoted geometry parameters are specified in Table I.
connects the gas-focusing region to the nozzle exit, was realized by a 30 μm circular orifice (400 shots, 50 Hz). The bridging section (layer 0) was written at 300 shots to ablate approximately half of the foil’s thickness. This ensures a steady gas stream while securing the side channel (SC) to the gas-focusing region during the hot embossing procedure. After laser ablation, the micromachined foil was sonicated in acetone for 10 min to remove any Kapton debris from the surface.

Hot press-assisted device bonding

Following the procedure described by Monteiro and co-workers,18 two Kapton FN sheets (i.e., 25 μm Kapton HN foil with a 25-μm-thick FEP coating) were cleaned with isopropanol and dried with pressurized air prior to use. The hot press was preheated to 270 °C, slightly above the FEP’s melting temperature. Surface roughening and activation of the cleaned parts were performed with a low-pressure plasma cleaner (50 W) at 0.38 mbar for 10 min. The device sandwich consisting of the laser-structured Kapton HN placed between two Kapton FEP foils was carefully placed onto the bottom hot plate. To avoid attachment of the device to the hot press, two Kapton HN sheets of 125 μm thickness were used. Kapton FEP bonding to the Kapton HN was performed using a series of consecutive steps, starting with a force of 1 kN for 20 s. To efficiently remove air bubbles, the pressure was first completely released for <1 s, followed by re-pressurizing with 1 kN force for 10 s. The cycle was repeated three more times, followed by a final press of 1 kN for 14 min. The bound device was removed from the hot press and allowed to cool to room temperature. The inlet ports were pierced through the assembly using a 0.4-mm hypodermic needle (Braun). Excess foil in the nozzle region was cut using a razor blade under the microscope. Figure 2 provides a schematic illustration of this procedure.

Liquid manifold and device mount

The Kapton nozzle was fixed into a custom, computer numerical control (CNC)-milled aluminum manifold (Figs. S1 and S2). The two sealing plates of the mount contained cavities to precisely position O-rings, which upon tightening the screws provided leak-free fluid connections to the Kapton channels. Two ports in the lower sealing plate provided access for pressurized gas, and a third port in the upper sealing plate connected the inner liquid line. The ports were machined with a No. 6-32 UNC thread for connecting suitable PEEK fittings. These threaded fittings contained 1/16” through holes for inserting PEEK tubings. In this manner, the inlets of the Kapton device were connected to gas-tight Hamilton syringes (upper sealing plate) and pressurized nitrogen (lower sealing plate), respectively. The syringes were driven using high-precision, pulsation-free syringe pumps. The gas line was provided by a PEEK tubing of 2 m length and 635 μm ID. The design of the sealing plates and device mount is provided as supplementary material files in the DWG and STEP format.

Liquid jet device operation

The microfluidic liquid jet devices were operated at liquid flow rates between 500 μl h⁻¹ and 10 000 μl h⁻¹ and at constant gas.
pressures between 0.5 bar and 2 bar. During operation, the gas flow is started first and then adjusted to the desired value. Next, the syringe pumps were set to the targeted flow rate for stable jetting. The imaging setup involved an inverse optical microscope and a focused xenon light source that allowed exposure times down to 0.3 \( \mu \text{s} \) when using a 20\( \times \) magnification objective and a 512 \( \times \) 32 pixel\(^2\) detection area (pixel size \( \sim 2 \mu \text{m} \)). The fast processes of jetting and droplet breakup were recorded using a high-speed camera capturing frames at a rate of 340,000 \( \text{s}^{-1} \). The jet diameter was measured via ImageJ at ten positions near the nozzle exit, \( \sim 100 \mu \text{m} \) into the jetting region (as indicated by black line in Fig. 3).

**RESULTS AND DISCUSSION**

**Design control and variation**

We previously reported on the use of pulsed laser ablation for the fabrication of microfluidic devices with 3D flow-focusing features. By transferring GDVN design parameters to this adapted micromachining protocol, we successfully fabricated inert polyimide-based liquid jet devices. With the trick of flipping the foil 90\(^\circ\), we were able to access the 125-\( \mu \text{m} \)-thick Kapton edge and ablate an orifice between liquid main channel and gas-focusing region (Fig. S5). Off-centered orifices could be eventually rectified through a test shot series elsewhere on the Kapton foil, which allowed an iterative improvement of the camera–laser position alignment. Once aligned, the centered orifice placement was highly reproducible and yielded homogeneous 3D gas-focusing for stable jetting. We pursued two geometric design variations: an inner orifice and outer orifice diameter set of ID:OD = 12:30 \( \mu \text{m} \) and 30:65 \( \mu \text{m} \), respectively. The small variation aimed for generation of fast liquid jets of a few \( \mu \text{m} \) diameter (with the smallest observed jet being 3.8 \( \mu \text{m} \)), while the larger aperture version is aimed to be compatible with a wide range of protein crystals, which according to the literature are usually between 5 \( \mu \text{m} \) and 20 \( \mu \text{m} \). In theory, the laser writing software allows microstructuring shapes down to 3 \( \mu \text{m} \) width. SEM images of the microstructured Kapton foils before and after heat sealing are shown in Fig. S6. The final structured channels and orifices were measured to be \( \sim 10 \mu \text{m} \) larger than the selected mask size. This deviation needs to be taken into account when planning future design iteration with the CAD software.

**Fabrication cycles**

The preparation time of the polyimide foil for laser micromachining (including focusing the laser onto the substrate) was \( \sim 10 \text{ min} \). With the utilized laser operation conditions, the (unsupervised) writing time of the microchannels for one GDVN was \( \sim 15 \text{ min} \). Further, implementing the liquid and gas aperture (including focusing) took additional 20 min. Moreover, it took 10 min for the sonication, 10 min for plasma activation, \( \sim 15 \text{ min} \) for hot embossing, and ten additional minutes for cutting and connection to the sample holder. Therefore, one invests merely 1.5 h for a complete iteration cycle from executing the CAD file until obtaining an employable microfluidic GDVN, which is much shorter than the 24-h “rapid prototyping” cycle described by Duffy et al., and, hence, represents a rather “extremely rapid prototyping” approach for the fabrication of microfluidic devices. Furthermore, the fabrication steps can be performed for up to five devices at once (laser

**FIG. 3.** (a) High-speed camera image of a polyimide liquid jet device (here: ID:OD = 12:30 \( \mu \text{m} \)) that focuses water (here: \( Q = 10 \text{ ml h}^{-1} \)) with pressurized gas (here: 0.5 bar \( \text{N}_2 \)) leading to a stable liquid jet with a jet diameter of 15 \( \mu \text{m} \) and a jet length of 840 \( \mu \text{m} \). The jet image (outside of the device) was taken at a frame rate of 340,000 \( \text{s}^{-1} \) and an exposure time of 0.3 \( \mu \text{s} \), while the rectangular image showing the internal nozzle geometry is captured at 93,000 fps and 1 \( \mu \text{s} \). (b) High-speed camera images (512 \( \times \) 32 pixel\(^2\) detection area, pixel size \( \sim 2 \mu \text{m} \), 0.3 \( \mu \text{s} \) exposure time, 340,000 fps) of the 12:30 \( \mu \text{m} \) (ID:OD) liquid jet with indication of the measurement range for the jet diameter (black solid line) and nozzle edge (white dotted line). The jetting length is controlled by the liquid flow rate. Here, a wide range of liquid flow rates between 0.9 \( \text{ml h}^{-1} \) and 10 \( \text{ml h}^{-1} \) are shown with a gas pressure of 1 bar and 0.5 bar, respectively.
ablation: successively, hot embossing: simultaneously) saving additional time. The main advantage of laser structuring in comparison with other GDVN fabrication methods is that it does not require time-consuming photolithography steps (cleanroom fabrication of master templates for PDMS nozzles) or overnight photoresin removals for 3D-printed nozzles. However, there are drawbacks of laser ablation: one cannot fabricate buried microchannels or write arbitrary features into the material as it is common for two-photon polymerization or selective laser etching.

Gas flow rate analysis

The gas flow rate of the operating microfluidic liquid jet devices in standard cubic centimeter per minute (SCCM) was determined as a function of applied nitrogen pressure (0.25 bar–2 bar) to obtain comparable values in relevant units and allow feeding flow controller software for high-fidelity operations. This determination was performed by putting the running microfluidic device under water and measuring the time until 25 ml of ejected gas was collected in a water-filled reservoir (in the absence of a liquid co-flow). The elapsed time was averaged over three measurement runs, and the results are shown in Fig. S3. The measured gas flow rates correspond to 19 mg min⁻¹–46 mg min⁻¹ (30 μm gas aperture) and 36 mg min⁻¹–104 mg min⁻¹ (65 μm gas aperture), respectively, and, therefore, should allow vacuum compatibility down to ~10⁻⁶ mbar.

Jet diameter control

Since the polyimide foil is transparent, the liquid flow and the meniscus could easily be observed and photographed at various positions along the flow axis. Figure 3 shows two merged photographs depicting the nozzle from the gas-focusing region to the droplet breakup regime and provides a series of high-speed images for the 12:30 μm (ID:OD) geometry at different liquid and gas flow rates. While investigating the 12:30 μm (ID:OD) devices, it was found that controlled liquid jet generation can be achieved when operating the nozzles at 0.5 bar and 1.0 bar (i.e., 19 mg min⁻¹ and 29 mg min⁻¹). 1.5 bar and 0.25 bar were also tested but did not result in a stable jetting behavior, rather than in whipping and dripping streams, respectively. In general and as expected, it was found that an increasing jet diameter is associated with an increased liquid flow rate. Moreover, smaller jet diameters were observed at higher gas pressures. Both observations are common features of GDVNs. A similar trend was observed with the 30:65 μm (ID:OD) device variation when a series of flow rates were tested at 0.5 bar and 0.25 bar. Here, no jet stability was achieved at 1.0 bar and 1.5 bar pressures where gas flow rates above 60 mg min⁻¹ are reached. Gañán-Calvo postulated an equation for the description of the liquid jet diameter, $d_j$, in his plate-orifice geometry,

$$d_j \approx \left( \frac{8\rho_l}{\pi^2 \Delta p_g} \right)^{1/4} Q^{3/4},$$

(1)

with $\rho$ being the mass density of the liquid ($\rho_{\text{water}} = 1$ g cm⁻³), $\Delta p_g$ being the difference of the applied gas pressure to the atmospheric pressure, and $Q$ being the liquid flow rate. Later, Trebbin et al. showed that this model can also be applied to microfluidic nozzle devices with rectangular channel cross sections. Fitting Eq. (1) to the herein reported experimental data with the incorporation of an additional scaling factor $c$ showed very good agreement of predicted/measured values (Fig. 4). The factor $c$ compensates for the flow rate of the focusing gas, which was not as accurately controlled as the liquid flow. Furthermore, Gañán-Calvo’s semiempirical formula is highly dependent on the setup and channel geometry. In general, the fitted curves differ from the expected values by 5%–15% as indicated by the factor $c$. Figure 4 provides jet diameter vs flow rate plots for different applied pressures based on the cumulative results obtained from the design variations together with the theoretical predictions.

The measured jet diameter further allows an estimation of the corresponding jet velocity, $v_j$, when assuming the dependence predicted by liquid flow rate and cross-sectional area of the jet,

$$v_j = \frac{Q}{\pi d_j^2},$$

(2)
with $Q$ being the liquid flow rate and $d_j$ being the jet diameter. Figure S4 shows that jet velocities of 30 m s$^{-1}$ can be achieved, which implies that the polyimide GDVN can provide jets fast enough for MHz data collection at XFELs. For instance, a minimum jet speed of 28.2 m s$^{-1}$ is calculated when assuming a displacement of $\Delta x = 25 \mu m$ between two adjacent x-ray pulses and assuming the source running at a 1.1 MHz pulse repetition rate, which can be encountered at the European XFEL.\textsuperscript{30,11,29}

**CONCLUSIONS AND OUTLOOK**

A robust GDVN liquid jet system was created from thin Kapton foils by using a highly reproducible UV laser ablation procedure from multiple angles. These 3D polyimide-based devices enabled the controlled generation of stable microjets with predictable jet diameters. Besides the reproducibility, another advantage of using Kapton is that it is contrastable to quartz crystals or UV-curable photoresists, it can be purchased at low costs. In fact, one sheet of Kapton HN (Detakta, 295 × 210 mm$^2$) was purchased for less than 25 euros and can yield ~600 devices, each 12 × 8 mm$^2$ in size.

Our laser structuring approach for GDVN fabrication provides chemically inert and temperature-resistant (up to ~250°C) sample environments that are highly resistant toward brilliant x-ray beams for in situ structural studies of dispersions before and after being jetted. Moreover, Kapton is highly suitable for high vacuum environments, which is vital to achieve very high signal-to-noise ratios in XFEL and long-wavelength experiments as the incident/transmitted beam is not scattered or absorbed by air molecules or device material sublimating away. Furthermore, this microstructuring approach could also be extended to other materials than Kapton (i.e., Mylar, TOPAS COC) and for the fabrication of other x-ray compatible sample environments such as fixed targets devices in the future.

Further advanced nozzle designs, such as double flow-focusing geometries or jet-in-jet mixing geometries for time-resolved experiments, and device adaptations to specific experimental conditions (beamline environments) can easily be implemented. Such solvent- and temperature-resistant GDVNs also offer great application potential for the solution blow spinning of micro- and nanofibers,\textsuperscript{5,19} and the aerosolization of liquids used, e.g., for single-particle imaging\textsuperscript{34} and cryo-electron microscopes,\textsuperscript{35} or for the generation of emulsion droplets and foams.\textsuperscript{36,32}

**SUPPLEMENTARY MATERIAL**

See supplementary material for more details about the device fabrication, the device holder, related CAD files, and additional experimental data about the device in operation.

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**DATA AVAILABILITY**

The data that support the findings of this study are available within the article (and its supplementary material).

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