Abstract: Smaller and denser micro-aperture arrays are opening up new applications in life sciences such as DNA sequencing, cell-based diagnostics, real-time PCR, tissue and bone repair. Excimer laser micromachining technology can simultaneously drill a large array of tightly-spaced ultra-small holes (1 to 2 microns in diameter) with consistent and repeatable hole diameter and pitch. The combination of drilling a large number of holes at one time and automated part handling makes laser micromachining a cost-effective technology platform to fabricate consumable devices in high volume.

The growing requirement for thin polymer membranes with dense micro aperture arrays

“Small is beautiful!” Many new, fast-growing technologies that affect our daily lives require ever-smaller features. Some examples of technologies that use micro-sized features include DNA sequencing, cell-based diagnostics, real-time PCR and tissue and bone rebuilding.

Specifically, the examples below show how some of these applications rely on micro-features:

i) New DNA sequencing methods require speed and low cost as they produce thousands or millions of sequences concurrently (4). Each sequence takes place on a tiny micro cell. PCR emulsion filters composed of dense micro-hole arrays help prepare the DNA sample or PCR-based molecular diagnostic analyte for bead-based assays.

ii) New PCR-based molecular diagnostic panel assays require micro-arrays of miniature bioreactors (blind wells) to test multiple tests at one time, saving time and costs.

iii) The clinical standard to repair human bone tissue and nerves is extracting them from another area in the body or from donors. The issues with these approaches include limited supply, pain, disease transfer, and the long time it takes for the body to adapt. However, by inserting a biodegradable polymer thin film with micro pores, not only can human bone tissue and nerves grow by themselves easily, but also the growth is controlled along the pattern direction of the micro features. (1)(2)(3)
Some applications require not only that the micro apertures are small and dense, but also that they are randomly distributed and have different diameters. For medical applications, micro-aperture precision, accuracy, and quality are especially important. Figure 1 shows a typical required micro-aperture pattern design.

![Figure 1. A typical micro-aperture pattern requirement, with random aperture distribution, aperture diameters from 4 to 8 microns.](image)

**Current methods to produce micro-apertures on polymer membranes**

There is a wide variety of techniques for making micro apertures on polymer membranes. However the real challenge is making dense micro apertures quickly.

Mass production fabrication methods include:

A) **Ion track etching:** Ion track technology uses high energy and heavy ions to irradiate the polymer membranes first and form deep linear damaged tracks (seeds) across the targeted polymer film, followed by a wet chemical etching process to produce micro apertures in the membranes. By controlling wet etching time, different micro aperture sizes can be achieved. This method is able to produce dense aperture diameters from submicron size to larger than ten microns. The advantages of ion track etching are fast process times and relatively low cost. The problem, however, is that it generates micro apertures in a random distribution and in random directions. Sometimes if two ion tracks meet each other, the overlap produces larger irregular-shaped apertures.

B) **Conventional lithographic and etching techniques:** This method has multiple steps including adding a photoresist coating, exposing the pattern, washing, plasma or chemical etching, and finally a photoresist removal process. It can produce defined distribution and very uniform apertures. But the cost is high and handling those thin polymer membranes is extremely difficult.
C) **Laser direct drilling**: Laser-drilling the apertures is a widely-used, mature manufacturing method. It is based on two mechanisms: heating-melting- evaporation and ablation or cold process. When the aperture diameter is less than 50 microns, cold laser ablation is selected where the laser photon energy directly breaks the bonds in the material within a thin top layer. It is a simple one-step process and is relatively low-cost, fast, and able to generate dense, one-micron diameter, controlled distribution and uniform apertures.

![Image](image.png)

Figure 2. Three 0.5 mm-wide channels connected to a 0.7 mm-wide channel with the depth of 0.15 mm on 0.25 mm thick PET sheet processed by controlled ablation using an excimer laser.

**Excimer laser excels at dense micro-aperture drilling**

For cold laser ablation, there are two methods: shorter wavelength, typically deep UV with higher photon energy, and short pulse duration with higher peak power, typically several picoseconds or less. Both have small heat effect zones, enabling the drilling of smaller diameter apertures to about 1 micron. The related typical optical configurations are mask projection and direct writing.

In direct writing, a picosecond or femtosecond laser beam (with a beam energy density that is Gaussian in profile) is first expanded and/or re-shaped and then focused on the surface of the target. The relative motion of the focused beam with respect to the target can be controlled either by scanning the focus spot (e.g., galvo or flying gantry system with smooth scanning speed greater than one meter per second) or by moving the target (e.g., stages with relatively low moving speed less than 0.05 meters per second), or by a combination of both.

To efficiently drill dense apertures and those smaller than 5 microns with direct writing, two critical conditions must be met: small focused beam and smooth, fast moving speed between the focused beam and the target. The Gaussian laser output beam requires a high numeric aperture focal lens (numerical aperture greater than 0.25) to form a focus spot smaller than 5 microns and a fast scanner. Today, it is still a challenge to design a scanner focal lens with a high numeric aperture and relatively large scan area. Also the intensity of the Gaussian
profile laser beams is higher at the center than at the periphery. This may result in over-exposure of the material in the center while the periphery does not receive sufficient energy. As a result, the apertures have no defined drilling edges and it is very difficult to drill dense micro-apertures consistently. It is impossible to drill micro-wells with smooth well bottoms. Even though there are some beam shape modification methods that convert Gaussian beams into flat-top beams of substantially uniform energy density, they may increase the efficiency of laser energy usage for relative large hole drilling, but not for holes smaller than 5 microns. Figure 3 (left) shows a UV picosecond laser-drilled aperture array on thin FEP sheet. The exit diameters are all approximately 7.5 microns but with some variability.

Figure 3. Left: An array of apertures drilled by a pulse width of 15 picoseconds with 355 nm wavelength laser on 0.012 mm-thick FEP sheet. Right: An array of apertures drilled by an excimer laser on a 0.012 mm-thick PEEK sheet.

On the other hand, excimer lasers have higher-order modes and produce quasi-uniform beams of relatively large cross-sections. They can be operated with UV or DUV wavelengths and employ a mask-projection technique. The laser beam is modified and then illuminated on a mask—which has the magnified desired target pattern—and then “imaged” by a downstream projection to form a smaller replica of the mask pattern on the target with higher energy intensity. For aperture drilling, the mask can be an array of thousands of apertures with random distribution and different aperture sizes. Since the illuminating beam intensity on the mask surface is highly uniform, the beam intensity on the target is highly uniform as well. Large numbers of multiple apertures, with random distribution and different aperture sizes (from 1 to 10 microns in diameter or other larger diameters) can be drilled simultaneously.

The mask-projection approach utilizes projection lenses with high numerical apertures. They can correct for optical distortion and aberrations and create high-resolution images on the target. This approach forms sharp aperture edges and enables the drilling of holes with consistent diameters with tight process control. Figure 3 (right) shows an excimer laser-drilled aperture array on a thin PEEK sheet. The exit diameters are around 7.5 microns and the diameters are very consistent.
**Typical high density 5 microns diameter or smaller apertures drilled on different polymers**

In order to drill holes smaller than 10 microns in diameter, it is necessary to have a high precision, uniform, sharp-edged features. When using an excimer laser with a mask with smaller than 150-micron features, a UV quality dielectric-coated quartz mask is required. By using a UV quality quartz substrate with a reflection coating created through traditional photoresist coating, pattern exposure, chemical etching, and coating removal processes, the outcome is a mask pattern with high positional accuracy, consistent opening size and sharp-edged features.

With the properly-designed quartz masks and an excimer laser micromachining system, apertures smaller than 5 microns can be drilled in a massively parallel fashion at a fast processing speed.

Figure 4 illustrates a microarray filter of holes of 1.0 micron in diameter drilled though a thin 0.025 mm thick polyimide sheet at a rate of 60,000 apertures per second.

![Figure 4](image1)

**Figure 4.** Exit diameter of 1.0 micron-apertures drilled on 0.025 mm-thick polyimide sheet. a) Top-left: Top illuminated optical microscope photo; b) Top-right: Bottom illuminated optical
microscope photo; c) Bottom-left: SEM pictures of larger array; d) Bottom-right: SEM detail of an exit aperture.

Figure 5 illustrates an aperture array in 0.008 mm-thick PEEK sheet. The 248 nm-wavelength excimer laser can drill over 170,000 apertures per second.

![Figure 5](image1.png)

*Figure 5. Exit diameter of 2.5 microns apertures drilled on 0.008 mm-thick PEEK sheet. a) Left: SEM pictures of larger array; b) Right: SEM detail of several exit apertures.*

Figure 6 illustrates an aperture array in 0.025 mm-thick PET tubes. The 248 nm-wavelength excimer laser can drill over 60,000 apertures per second.

![Figure 6](image2.png)

*Figure 6. Exit diameter of 5.0 micron-apertures drilled on 0.025 mm-thick PET tubes. a) Left: SEM pictures of larger array; b) Right: SEM with larger view of exit apertures.*

**Opening percentage relative to hole diameters**

Many life science applications not only require the smaller apertures but also need to control the aperture opening percentage (the total aperture open area versus total sheet area). It is relatively easy to have a low percentage aperture opening which means few apertures. However it is always a challenge to have high-percentage aperture openings. A typical laser-drilled aperture has a taper profile where the entrance diameter is larger than the exit diameter.
The taper angle depends on the laser parameters, optical set up and material properties. Typically, the half taper angle is between 3 to 10 degrees. As a general rule, the thicker the material, the smaller is the taper angle. This taper angle limits the density of the apertures. In order to have a clear entrance land between apertures, the aperture-to-aperture pitch distance has to be larger than the aperture entrance diameter. For a given pitch distance, hexagon aperture array displacement will maximize the aperture opening density.

The calculation and comparison of hexagon displacement and square displacement is illustrated in Figure 7. For a hexagon layout, the total area could be totally covered with multiples of the blue triangle shapes. The total aperture opening could be represented by the blue triangle. Assuming the aperture diameter is D and the gap between apertures is Gap (as shown on Figure 7 (left)), the triangle area is:

\[
\text{Aera}_{\triangle} = (D + \text{Gap})^2 \times \sin(60^\circ) / 2
\]

The opening area within the triangle is:

\[
\text{area}_{\text{opening}} = \pi D^2 / 4 / 2
\]

So that the opening percentage is:

\[
\text{Percentage}_{\text{Hexagon}} = \frac{\text{area}_{\text{opening}}}{\text{Aera}_{\triangle}} = \frac{\pi D^2}{((D + \text{Gap})^2 \times 4 \times \sin(60^\circ))} = 1.1547 \times \frac{\pi D^2}{((D + \text{Gap})^2 \times 4)} \quad (1)
\]

With a square layout, the total area could be totally covered with multiples of the blue square shapes. Therefore, the total aperture opening could be represented by the blue square. Again, assuming the aperture diameter is D and the gap between apertures is Gap (as shown on Figure 9 (left)), the triangle area is:

\[
\text{Aera}_{\square} = (D + \text{Gap})^2
\]

The opening area within the square is:

\[
\text{area}_{\text{opening}} = \pi D^2 / 4
\]

So that the opening percentage is:

\[
\text{Percentage}_{\text{Square}} = \frac{\text{area}_{\text{opening}}}{\text{Aera}_{\triangle}} = \frac{\pi D^2 / 4}{((D + \text{Gap})^2 \times 4)} \quad (2)
\]

Therefore the hexagon displacement has 1.1547 times opening density compared to the square displacement.
Using the hexagon displacement, if we use the gap distance of 9 microns, applicable for most thin polyimide sheets, the opening density versus aperture exit diameter is shown in Figure 8. From the aperture exit diameter of 1 micron to 100 microns, the opening density could vary from under 1 percent to over 70 percent.

Laser drilling apertures less than 5 microns on thicker material and depth control drilling

Some new life science applications require not only high density and smaller apertures but also high mechanical strength, necessitating thicker materials. Another requirement is micron-wells instead of through apertures. Both requirements bring new challenges which can be addressed by an excimer laser, an optimized optical system and suitable process parameters. Figure 9 shows a high density 2.5 micron-exit aperture array on 0.075 mm-polyimide sheet and Figure 10 shows a cross-section of the depth controlled micron-wells.
Figure 9. Exit diameter of 2.2 microns apertures drilled on 0.075 mm-thick polyimide sheet.  
a) Left: SEM pictures of larger array; b) Right: SEM detail of an exit aperture.

Figure 10. Cross-section view of depth control apertures drilled on 0.075 mm-thick polyimide sheet.  
a) Left: Micro-well with the bottom thickness of 15.9 um; b) Right: Micro-well with the bottom thickness of 10.4 um.

Conclusion:
Smaller and denser micro-aperture arrays are opening up new applications in life sciences such as DNA sequencing, cell-based diagnostics, real-time PCR, tissue and tissue and bone repair. Laser micromachining technology offers advantages over ion track etching and conventional lithography. Excimer laser-based micromachining excels at drilling tightly-packed, dense micro-hole arrays in various polymer films with the advantages of a scalable, cost-effective manufacturing platform producing consistent, repeatable features.

