IV. Frequently Asked Questions: Fabrication and Characterization

1. Do I have to use vacuum exposure to photo-polymerize hydrogels?
   Oxygen presence can quench photo-initiators[4-5] and prevent hydrogel forming. But it is not universally required to perform exposure in vacuum.
   For bulk hydrogels (a few hundred μm thick), vacuum exposure is not necessary for bulk as oxygen concentration in liquid decreases with depth [9].
   For thin-film hydrogels (μm-range hydrogels), it is also not always necessary to do vacuum exposure. For instance, PEG-based hydrogels can be exposed in air [10].
   For HEMA-based hydrogel, μm-range hydrogels is hard to be photo-polymerized in air and vacuum-mode exposure is necessary (Figure 1)

2. How does vacuum exposure work in SNF?
   See Figure 1. First spin coat hydrogel on the wafer. Next, bring the wafer on the Karlsuss. Make sure to select the chuck that with tubing ring surrounding it. Finally select vacuum exposure mode on Karlsuss. During vacuum exposure mode, the tubing is inflated, forming a chamber that encloses the wafer. The chamber will be purged with nitrogen and pumped to vacuum through the grooves on the chuck holder.

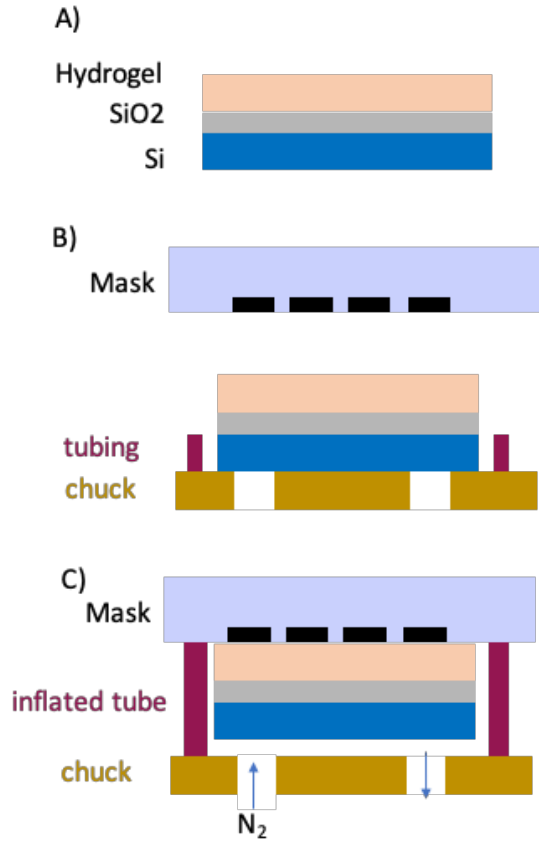

Figure 1. Illustration for vacuum exposure in SNF with Karlsuss.

3. Any alternative method that doesn't require vacuum exposure?
   We attempted to replace vacuum-mode exposure on Karlsuss with another method shown in Figure 2. First, spin coating the HEMA hydrogel in a nitrogen glove box, cap it with a mylar film to block air contact, and then take the capped wafer out of the glove box to align and expose in Karlsuss. This method is inspired by [11]. However, the diffraction from the mylar film spacer is too severe, even with the thinnest mylar film available from vendors (25 μm). The hydrogel film is either not crosslinked or overly exposed and all patterns are merged together due to mylar film diffraction.

   If no alignment is needed, you can directly cap the hydrogel with a transparency mask in Figure 2B, and then expose in UV-cure. This works well as no space layer is between the mask and the hydrogel, and the resulting resolution is high.

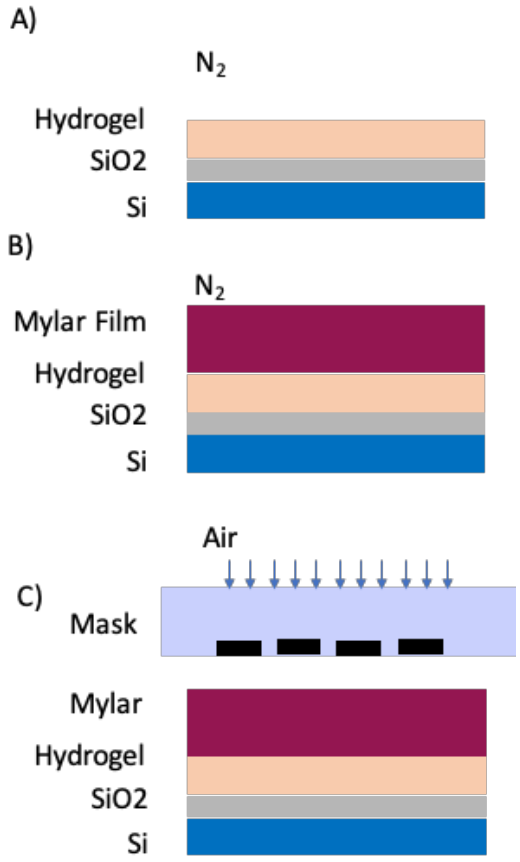

Figure 2. Illustration of mylar capping method.

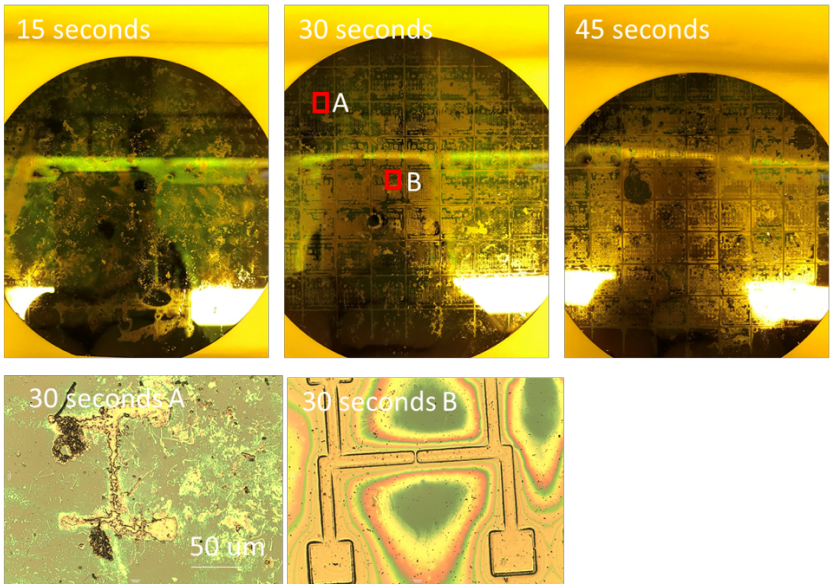

Figure 3. (Top) HEMA-DMAEMA exposure result on 4-in Si wafers with the mylar film capping method exposed at various times. (Bottom) On the same wafer hydrogel is either not crosslinked or over exposed.

4. How to do intermittent exposure?
   On Karlsuss, turn on “Multiple Exposure” light on the keyboard. When editing program, adjust both the “Exposure Time” [sec], “Wait Time” [sec] and “Number of Exposures”.

5. Why do we use intermittent exposure?
   Hydrogel prepolymer diffuses during exposure and may lead to irregular shapes around the hydrogel edge[11-12]. Detailed explanation can be found in [12]. At a high level, the radicals from photo-initiators are generated in large quantities in the light-exposure region and can diffuse toward the light-off region. The monomers on the other hand, have a lower concentration in the light-exposure region as they are being consumed to crosslink to polymers. The monomers can diffuse from the light-off region toward the light-exposure region then. Therefore, shape irregularities may form at the boundary between light-exposure and light-off.
   Depending on the level of diffusion, this intermittent exposure may not be universally required for all types of hydrogel.

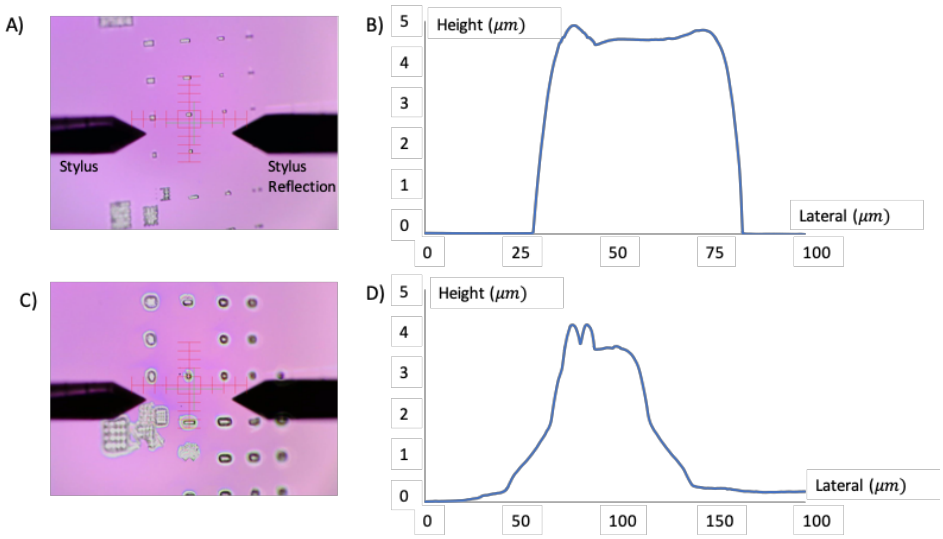

Figure 4. Representative sample images of intermittently exposed hydrogels (A) and profile images (B). Image of continuously exposed hydrogels (C) and profile image (D). The profiles are measured in Dektek Profilometer in SNSF, hence the images show the Dektek stylus (Question 9).

6. My hydrogel is over exposed, why is that?
   In addition to too long exposure time, it can also be due to diffusion and dark polymerization[12]. To minimize diffusion, you may try intermittent exposure. For HEMA/DMAEMA hydrogel [3] experimented at here, I usually use a duty cycle of 1 second on and 7 second off. Please note, this duty cycle is not fine-tuned for best resolution or repeatability. The chemical mixture process can have high run-to-run variations and the Karlsuss light intensity is also not perfectly constant over time. Therefore, this number is just a starting point.
   The free radicals retain some energy even after the light is off and may continue inducing polymerization [13]. Thus, it is recommended to rinse the wafer repeatedly immediately after the exposure.

7. Can I do nitrogen bubbling instead of vacuum exposure?
   Nitrogen bubbling is the process of purging out oxygen by bubbling nitrogen through the liquid (Figure 5). While an effective method for bulk fabrication, it doesn't make a difference for thin film process. Even if the pre-polymer is free of oxygen after the nitrogen bubbling, oxygen quickly diffuses through the thin pre-polymer film during spin coating.

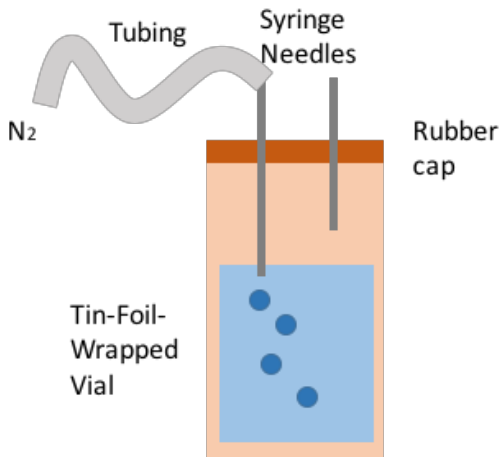

Figure 5. Nitrogen bubbling setup illustration. Nitrogen enters through a needle to the liquid, and exit through another needle. It is important that only 1 needle is in the liquid, otherwise the liquid will be pumped out through the other needle. The vial is enclosed with an elastic rubber cap where needles are punched through. The vial is wrapped in tin-foil to prevent polymerization with ambient light.

8. Inhibitor removal?

Often, acrylates monomers come with MEHQ (Mequinol) to inhibit radical polymerization. And it is recommended to slowly pass monomers through alumina beads to remove inhibitor. Sigma-aldrich sells glass columns pre-filled with beads, but it is for large amount of chemicals (hundreds of mL). To save materials, it is easy to pour out the beads from the glass column and build a smaller column with syringe (Figure 6). It was found that reveals that his trace amount of inhibitor didn't affect our experiments. Preliminary experiments show no difference between monomer as received and monomer with inhibitor removed.

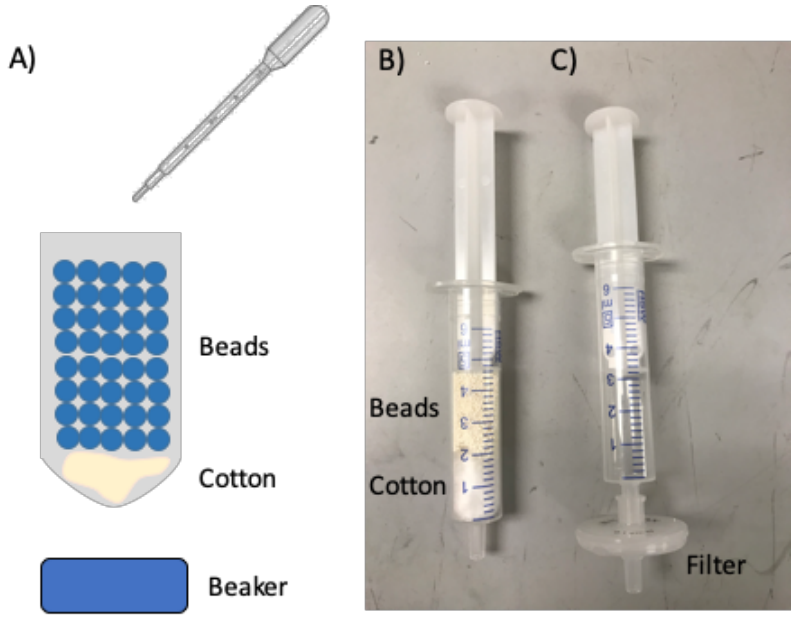

Figure 6. Inhibitor removal process setup illustration (A). Use a syringe, fill the bottom with a thumb nail-sized cotton piece, and fill the rest of the syringe with alumina beads (B). Slowly add monomers in the

syringe. You may need to squeeze from the top to help liquid to pass through the column. Finally, collect the liquid in the beaker and pass through a syringe with filter to remove any particles (C).

9. How to characterize hydrogel height?
   The most convenient method is using Dektek profilometer in SNSF (Figure 4). Select the minimum amount of force (1mg) to prevent hydrogel from being indented by the stylus. The data is comparable with AFM result (in question 9).
   I've experimented with the Keyance laser confocal microscope in SNSF. It is very challenging to adjust the setting to get reliable measurement for hydrogel (μm range thickness).
   Although hydrogel cannot be left in air for an extended period of time (see question 12), it's okay to leave HEMA/DMAEMA hydrogel can be in air for up to 2 hours during measurement.

10. How to characterize hydrogel thin-film swelling dynamics?
    It is recommended to first characterize the bulk piece swelling behavior to verify the hydrogel responsiveness to the stimuli. Typically you can immerse the hydrogel in the analyte, and then measure its weight.
    The best way to directly characterize hydrogel swelling dynamics at thin film level is using BioAFM in the Shriram cell facility. That is the only profile measurement tool that allow sample to be submerged in water. California weather is dry and water can quickly evaporate from thin film hydrogels, therefore, swelling dynamics can only be measured when hydrogel is actually submerged in water. See Figure 7 for sample result.

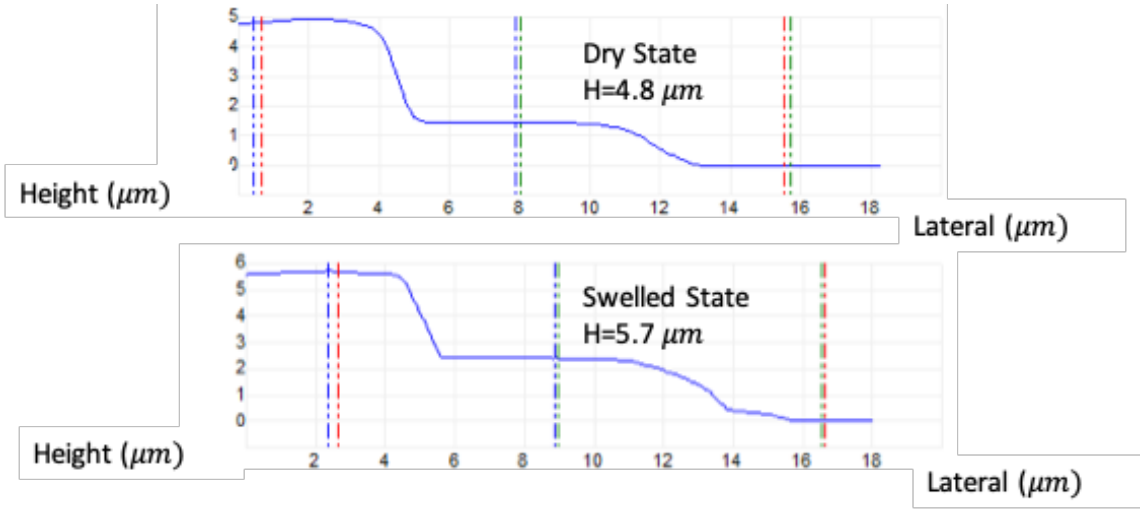

Figure 7. Hydrogel height measured in BioAFM. Height increases 20% transitioning from temporarily being dry and in water.

11. My bulk hydrogel weight has decreased in DI water, why is that?

    There can be a few reasons why your hydrogel weight can be decreased instead of swelling in DI water.

    a. Solvent crashing out

       To dissolve non-water soluble chemicals such as DMPA, sometimes we add IPA or ethylene glycol as another solvent. We may also add ethylene glycol to increase water uptake ratio in the hydrogel [3]. Hydrogel composite polymers may have hydrophobic part, and ethylene glycol is a type of hydrotrope which can improve solubility of hydrophobic substances in water. When these hydrogels are immersed in water for the first time, IPA or ethylene glycol will crash out due to the drastic concentration imbalance inside and outside of the gel (Figure 8). Crashing out can be prevented by dialysis: slowing change the analyte solvent ratio from a combination of water and the other solvent to purely water. Usually a 10% step is good.

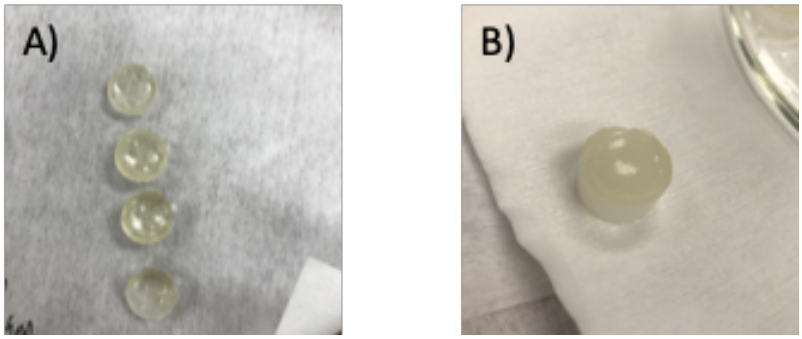

Figure 8. HEMA-DMAEMA hydrogels containing PEG. Immediately after cross-linking (A) and immersed in DI water for 2 hours. The hydrogel looks cloudy as ethylene glycol “crashed out”. This can be prevented by dialysis.

    b. Un-reacted materials

       Un-reacted monomers may leach out. Photo-initiators are not part of the hydrogel network and will leach out too.

12. My bulk hydrogel is not swelling/shrinking responding to environmental changes, why is that?

    To name a few possible causes: a) Hydrogels are dried out too much, breaking covalent bonds, which is irreversible. b) Hydrogels chemical crash out in water, irreversibly breaking covalent bonds in the structure. c) Hydrogel phase separates. It has too much or too little water. The hydrogel is may not be mixed well enough. The polymer/water ratio in the recipe may need modification.

Figure 9. Hydrogel completely dried after being in air for 3 days and shows “trenches”.