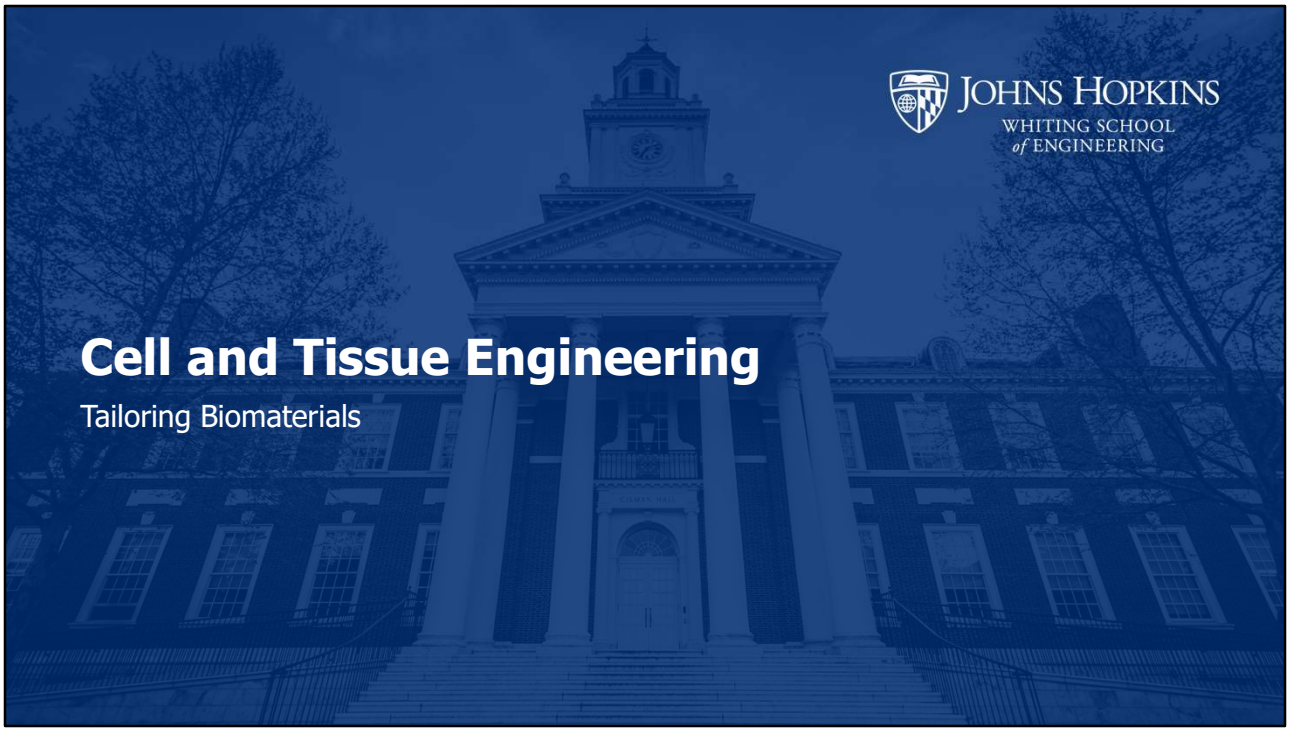


Cell and Tissue Engineering

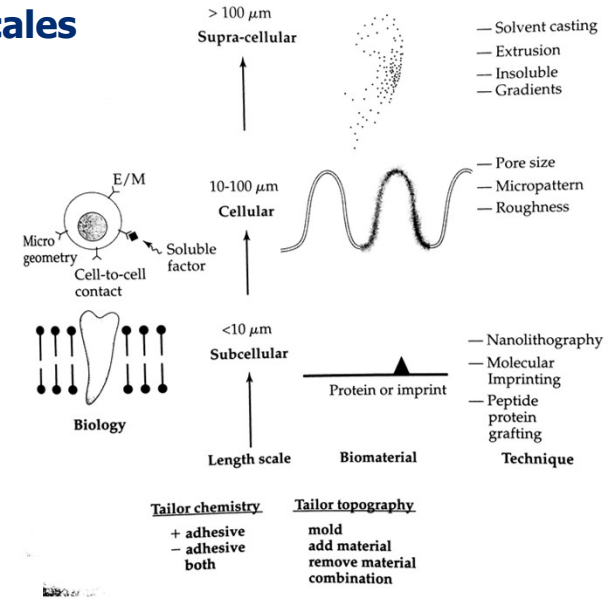
Tailoring Biomaterials

Tailoring Biomaterials - Scales

Subcellular length scale (<10μm)

Cellular microenvironment (10-100μm)

Supracellular structures (>100μm)



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2

Biomaterials are rarely used "**off the shelf**" so to speak. They are tailored to meet the needs of the project or tissue at hand.

This can be done at three length scales ranging from **sub-cellular** to **supra-cellular**.

On the right I'm showing you a diagram of strategies used for tailoring all along this continuum.

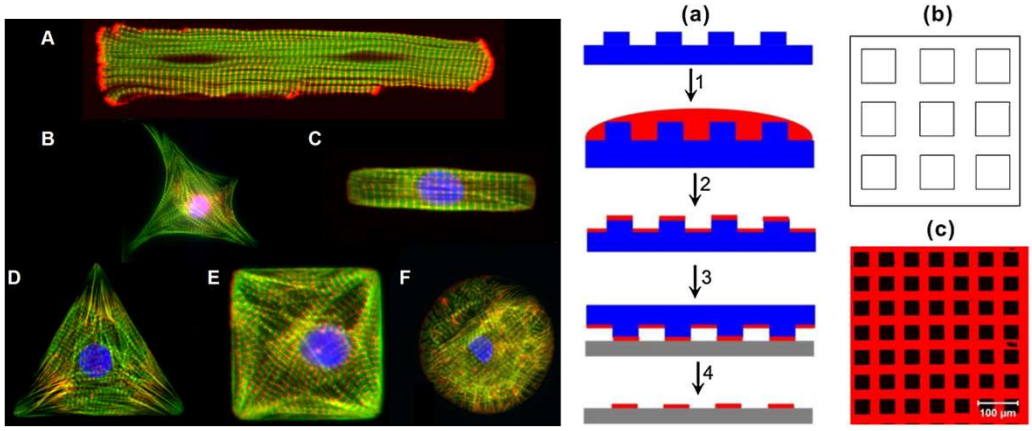
If we start at the **bottom** we see **surface chemistry** and **topographical tailoring** at the subcellular length scale, then more size and **micro-patterning** at the cellular length scale and finally **solvent casting** at the supracellular length scale.

In this talk we'll only cover 1 of these strategies and you can read about the others in your supplied reading this week.

So here we'll be highlighting the use of micro-patterning techniques for tailoring on the cellular scale.

Tailoring Biomaterials – Micropatterning (1)

Mechanical Controls: Shape



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3

You may remember this image from Module 5 when we discussed controls of morphogenesis. We also saw this technique used for directed migration in module 7.

Micro-patterning or **microcontact** printing is a tool that allows you to control how adhesive or other proteins are arranged. In doing so you can control where cells are placed. As you can see here – cells were adhered to theses areas but not in-between. This is because there are only adhesive proteins on the substrate here.

By regulating the areas of adhesion you can control **cell shape** and phenotype (you may remember the example of MSC modulating between bone and adipose tissue,) you can **control where cells migrate with tracks**, as well as proliferation rates and protein expression.

You can also use micro-patterning to arrange the relative locations of more than one cell type, in essence building a tissue one cell at a time.

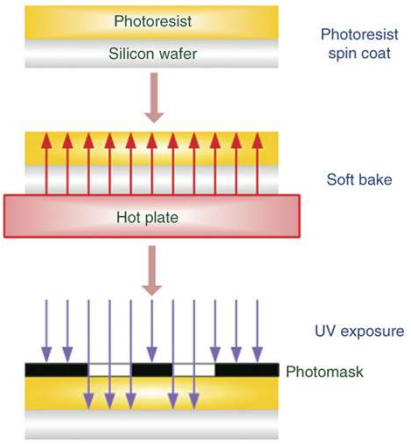
Clearly this technique is a very powerful one for tissue engineering purposes.

Previously we discussed how you start with an elastomeric stamp that you can ink in a protein solution and use to literally stamp out adhesive areas.

What we didn't discuss is **how** you make that stamp

Tailoring Biomaterials – Micropatterning (2)

Photolithography creates 3D patterns in polymers



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4

Geng et al 2011

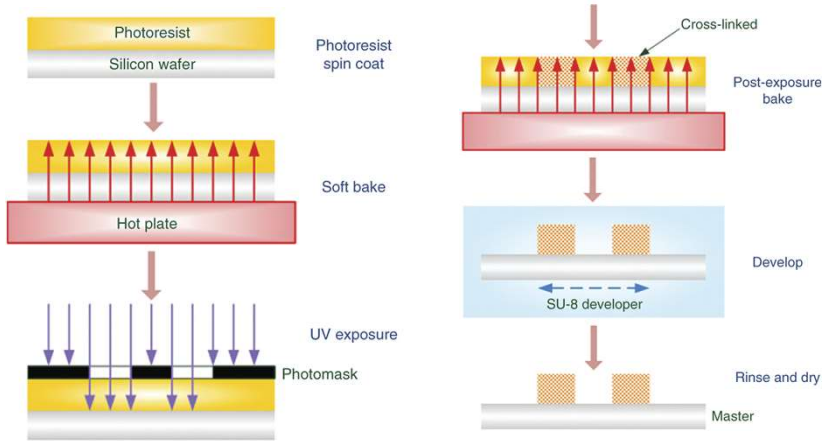
The process to make the 3D stamp is called **photolithography**. We'll go over that here but you can learn it hands on by taking our lab course in microfabrication.

It begins with a silicon wafer. You can see one here held by one of the VPs at Intel showing off the world's first chip printing 22 NANOMETER features in 2009. That wafer is covered with trillions of memory cells all made using lithographic methods.

The method beings with a silicon wafer like this one – it is coated with a liquid material called photoresist that is baked to set solid. A mask is designed with the pattern you want used to allow and **restrict** light onto the photoresist layer.

Tailoring Biomaterials – Micropatterning (3)

Photolithography creates 3D patterns in polymers



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5

Geng et al 2011

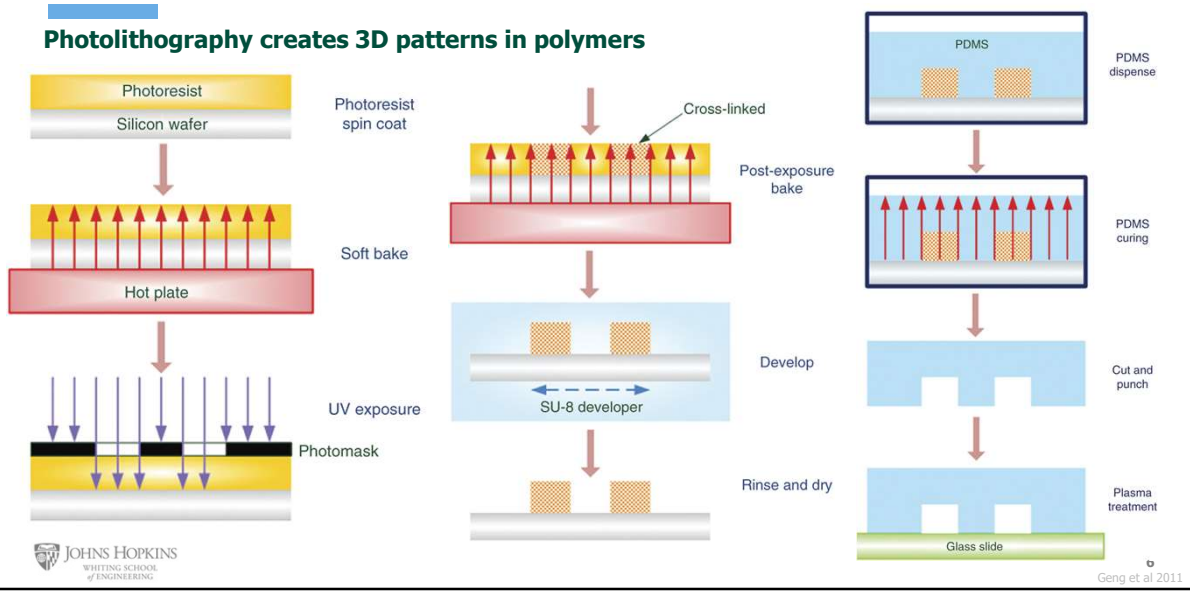
Another bake step crosslinks **photoresist** in the areas that were exposed to light, and developing agent that is specific to the photoresist is used to remove the unexposed, uncrosslinked resist.

This is an example of a positive resist – there are also negative resists which do the opposite and cross link in the areas not exposed to light.

As you can see you are left with 3 dimensional features of photoresist. The **height** of the features depends on the thickness of the initial photoresist layer.

Tailoring Biomaterials – Micropatterning (4)

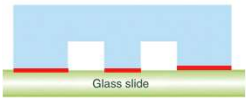
Photolithography creates 3D patterns in polymers



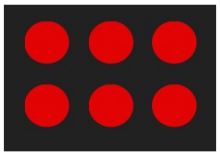
Finally the wafer + resist is used as a mold to cast an elastomeric stamp. After pouring the liquid elastomer onto the mold, it is cured and then released leaving you with a stamp.

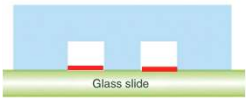
Tailoring Biomaterials – Photolithography

Photolithography creates 3D patterns in polymers

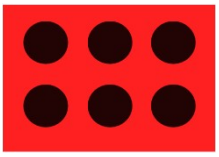


Print directly with the stamp





Microfluidic patterning



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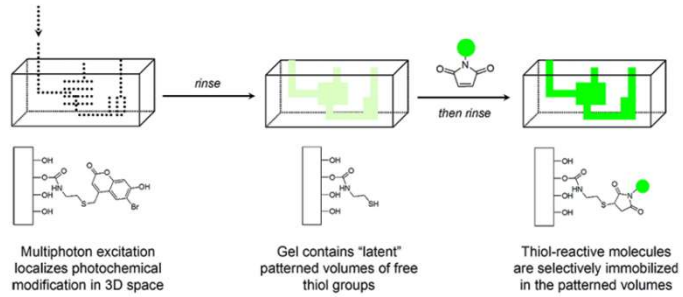
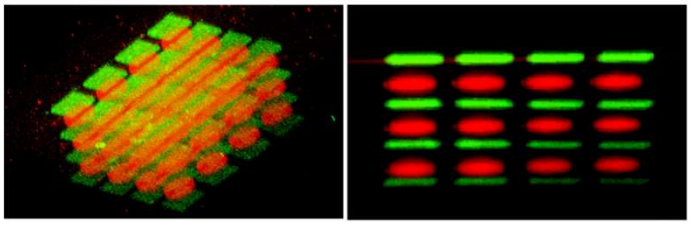
7

You can use the stamps in a variety of ways – to print proteins directly or to inversely print materials via microfluidic patterning.

In the latter method the stamp is placed in contact with the substrate – a glass microscope slide in this case and then a protein solution is flowed through the channels. When the stamp is removed the areas where it contact the glass show no protein.

Tailoring Biomaterials – Patterning in 3D





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8

Santos et al 2011

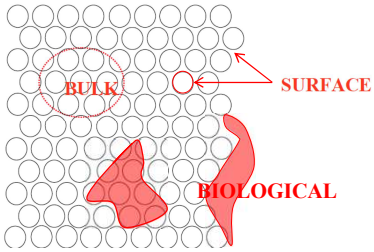
This method isn't restricted to 2D surface. There are several techniques that use lithography to pattern 3D features into 3D gels.

In this case a multiphoton laser beam is used for exposure. This beam can be focused not only in the **xy plane** but also in z-direction, affording you control of crosslinking or modification to the hydrogel in the third dimension.

In this example, you can see the excitation functionalizes the areas of the gel that it reaches so that when a protein solution is rinsed through only those areas adsorb it. By repeating the process serially, you can create 3d patterns of different proteins – red and green shown here.

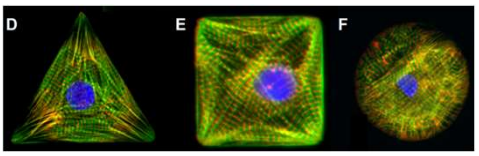
What do we know?

Biomaterial Properties



Biomaterial Types

Tailoring Biomaterials



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9

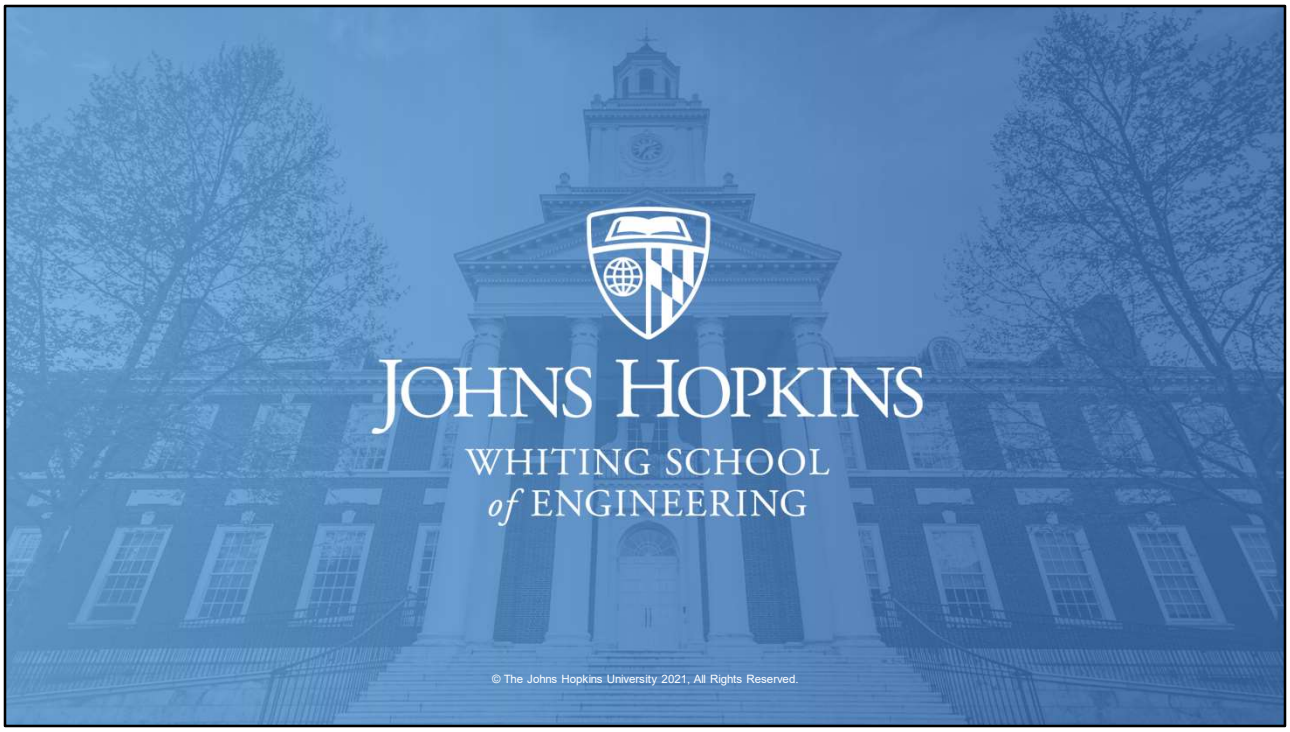
Let's review what we're learned so far

We talked about biomaterial properties – surface wettability
Bulk crystalline structure
and biocompatibility

We also discussed types of biomaterials – biological and synthetic materials. We went over some of the main players and their attributes.

Finally we saw some of the ways we can **tailor** biomaterials at 3 different length scales – sub cellular, cellular and supra-cellular. We specifically focused on the use of **lithography** to create 2d and 3d patterns at the cellular scale.

Next up we'll talk about integrating these materials into a host and dealing with biocompatibility.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