An Introduction to 3D Bioprinting

Lesson goals

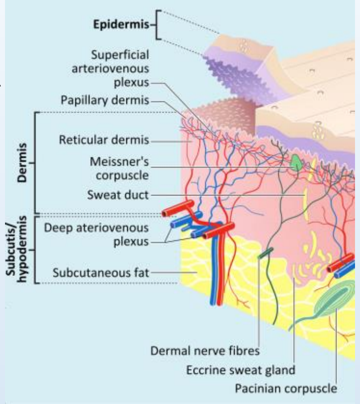
- Introduce engineering problem ("Bill")
- Define and analyze different types of 3D bioprinters
- Define the basics of tissue engineering
- Identify current applications and limitations of 3D bioprinting
- Start figuring out how to help Bill!

Why do we care about 3D bioprinting?

Watch this video

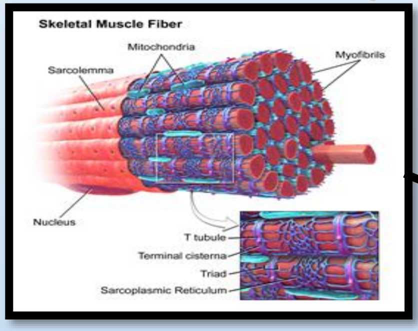
Bill’s Injuries

Image 1



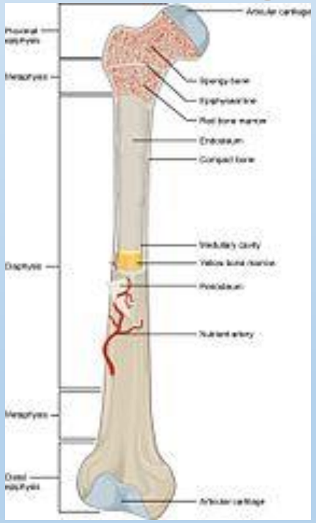
Missing skin on the left arm

Image 2



Ripped rectus femoral muscle

Image 3



Severely broken femoral shaft

We need ***your*** help!

Image 4

What is 3D bioprinting?

Image 5

Image 6

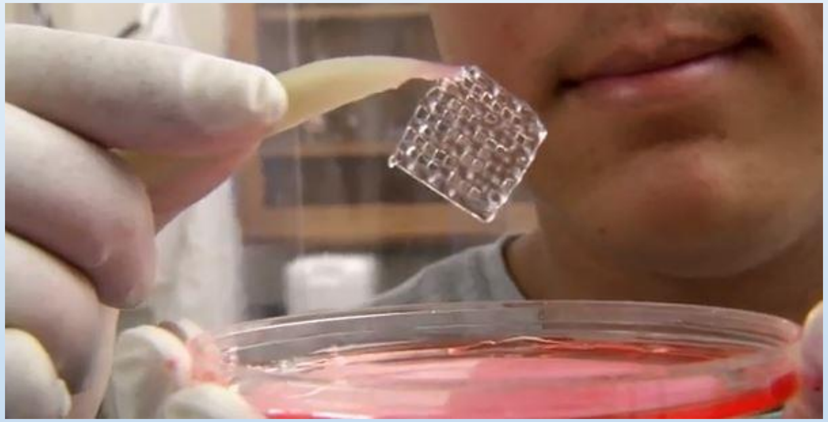


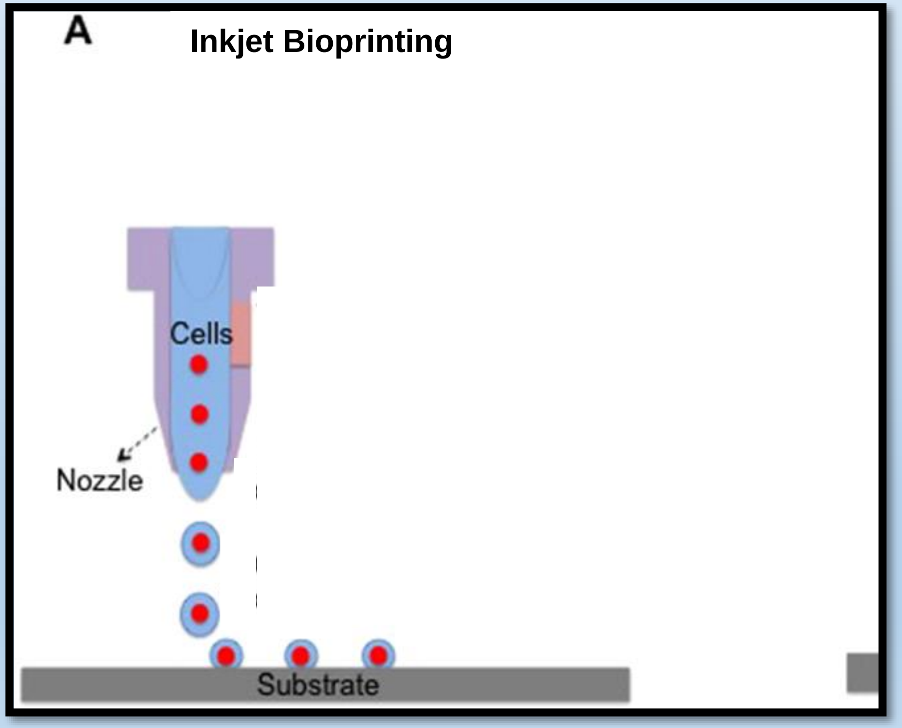
Image 7

We need to learn about the different types of bioprinters!

Will be used in the activity

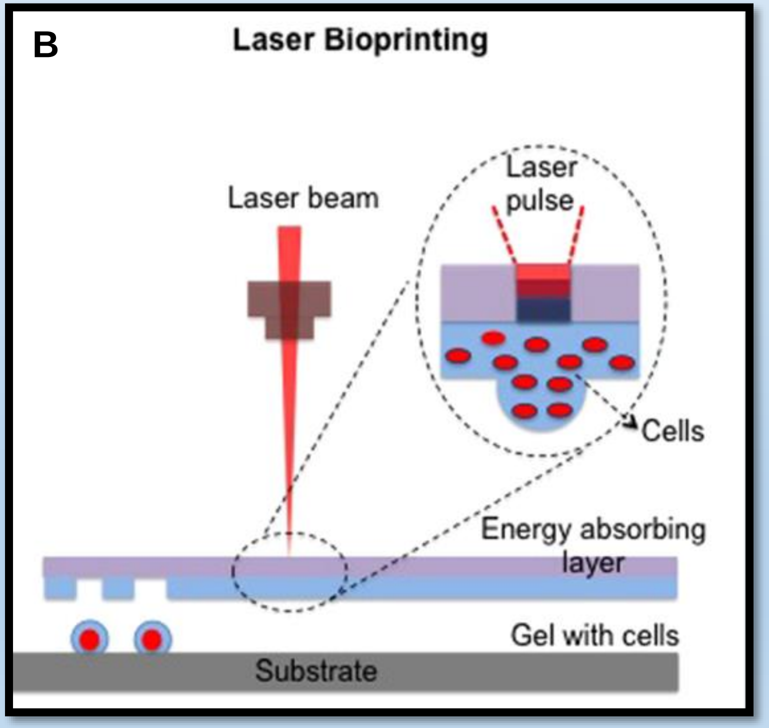
inkjet

Image 8



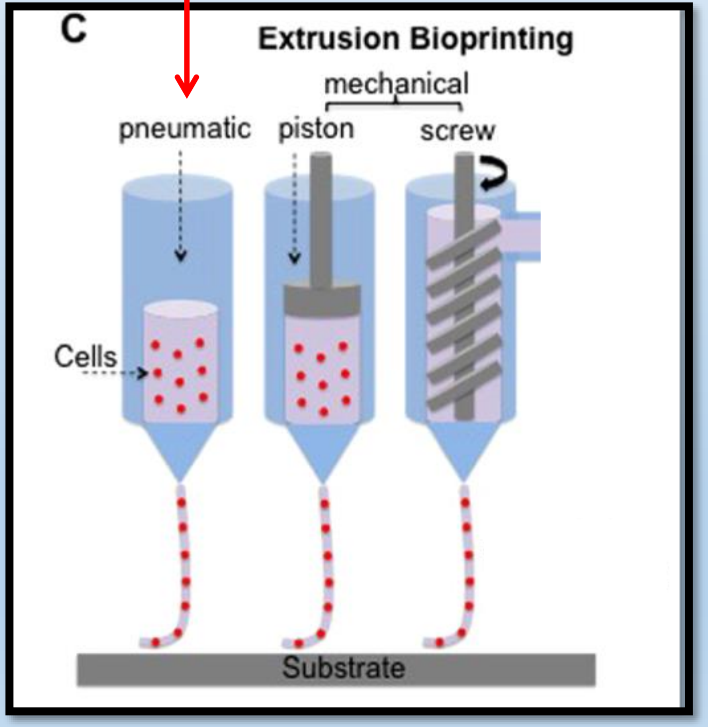
laser

Image 9



extrusion

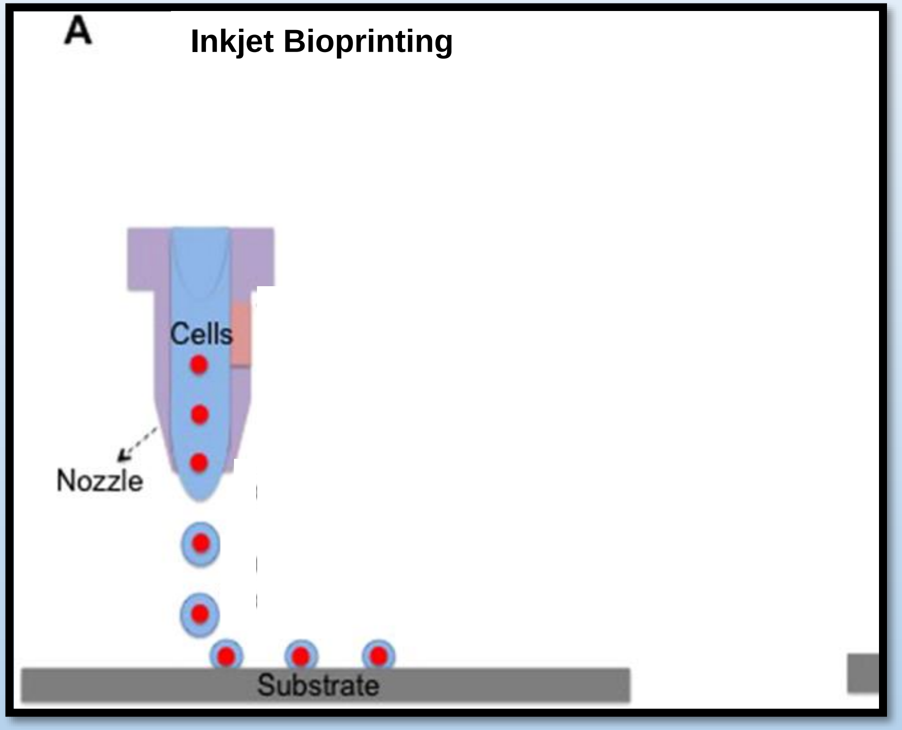
Image 10



Types of bioprinters: Inkjet

- Analogy: inkjet printer
- Limitations
  - Low viscosity
  - Bio-ink must solidify
  - Cell densities

Image 8



- Best application = quickly creating skin grafts

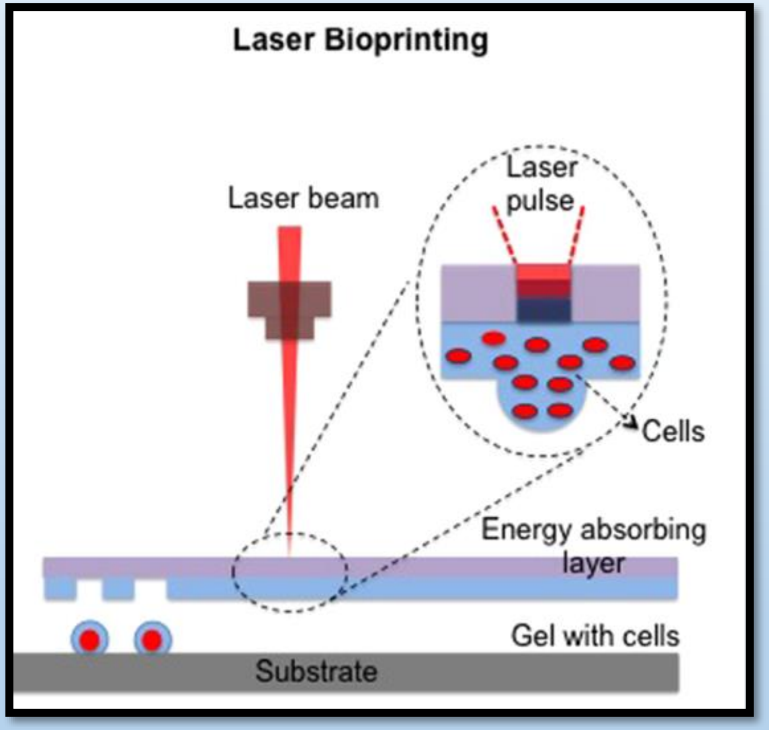
Types of bioprinters: Inkjet

Watch this video

Types of bioprinters: Laser Assisted

- Analogy: placing polka dots on a dress to create a pattern

Image 9



- Limitations
  - Low printing speed
  - Cannot print multiple layers easily
  - Wasteful

- Best application = placing cells precisely into solid structures

Types of bioprinters: Laser Assisted

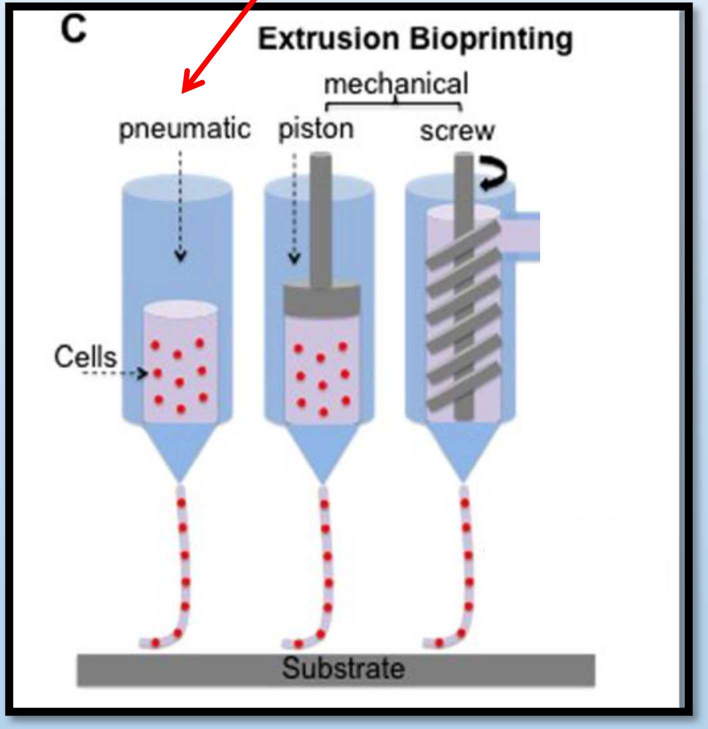
Watch this video

Types of bioprinters: Extrusion

Will be used in the activity

- Analogy: squeezing ketchup out of a bottle

Image 10



- Limitations
  - Lower cellular viability
  - Low resolution
  - Slow print speed

- Best application = creating large 3D structures

Types of bioprinters: Extrusion

Watch this video

Parts of an extrusion bioprinter

Reservoir 2

Image 11

Reservoir 1

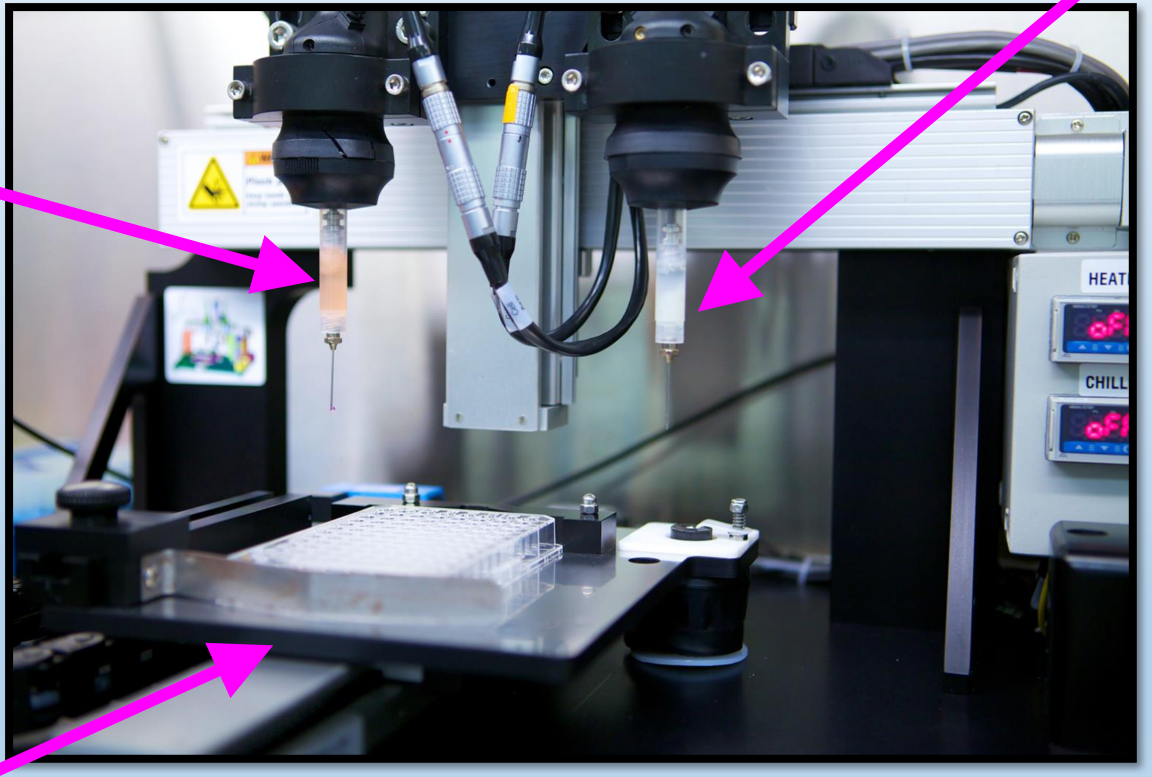


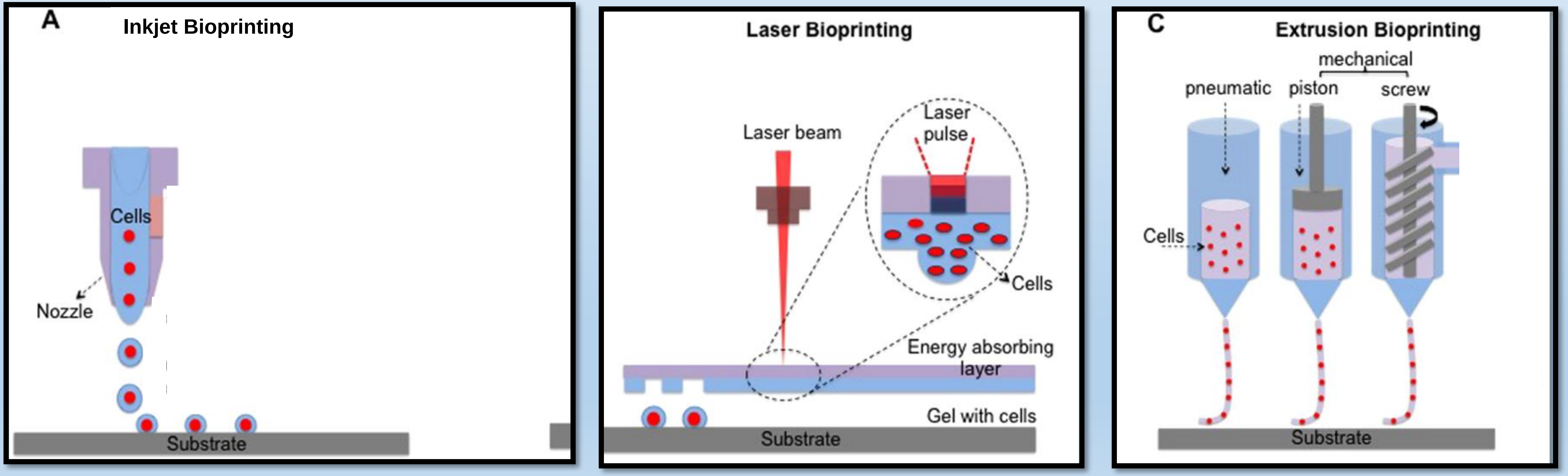
Image 11

Printing stage

+ Control system

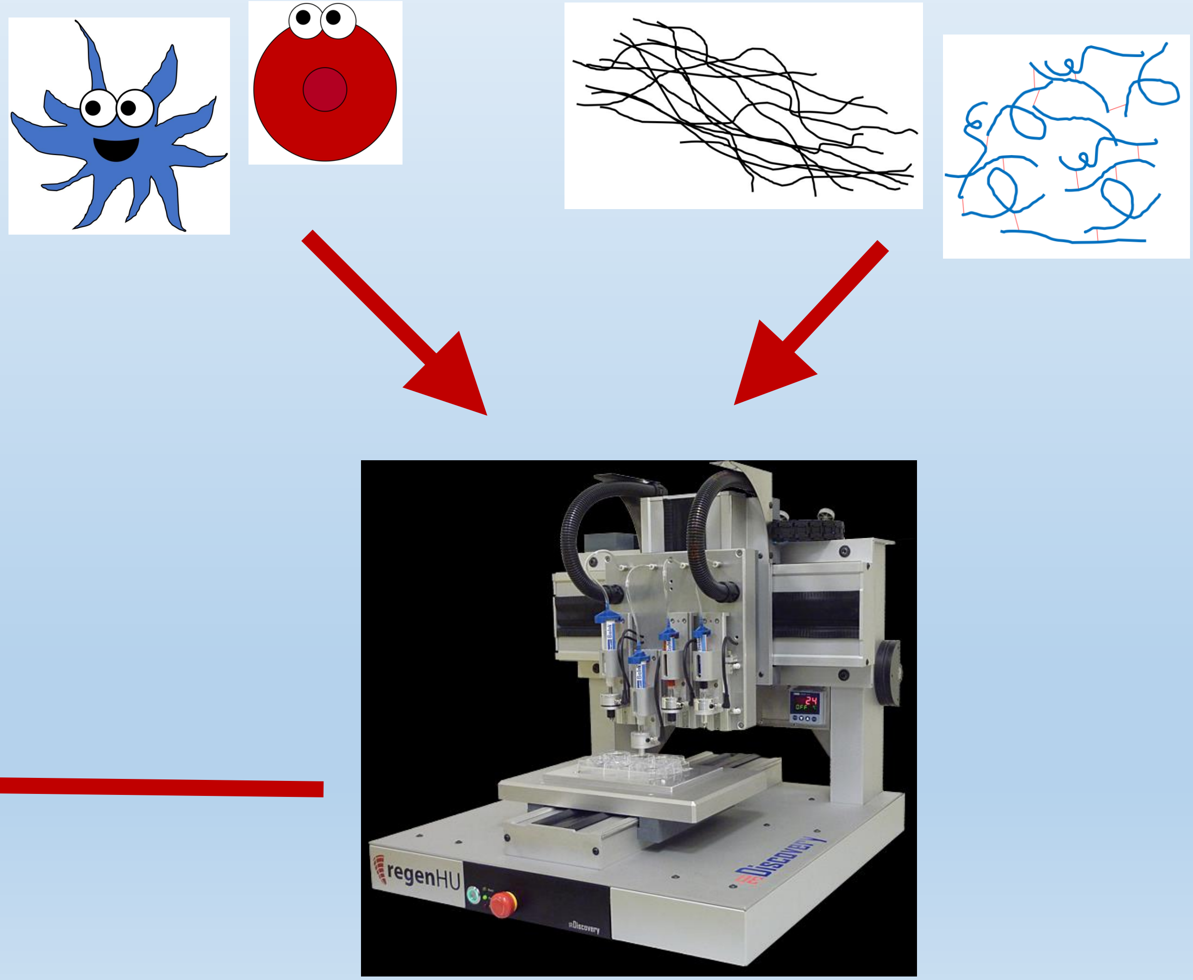
Types of bioprinters: Summary

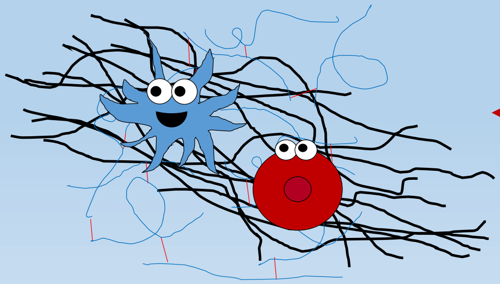
inkjet | laser | extrusion



Basics of tissue engineering design: 5 Steps

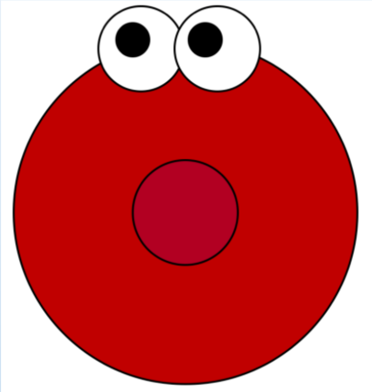
1. Identify function being replaced
2. Determine cell types
3. Determine biomaterial types
4. Determine construction method
5. Construction!



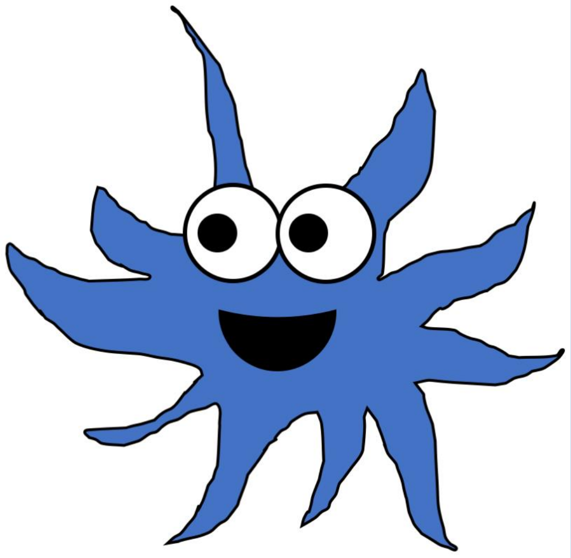


Determine cell types

- Choose cell type for its **function**!

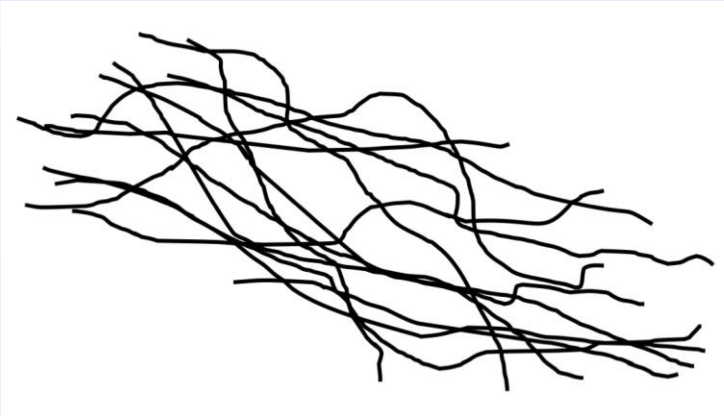


- Constraints:
  - Strength of cells
  - Rejection and immune responses

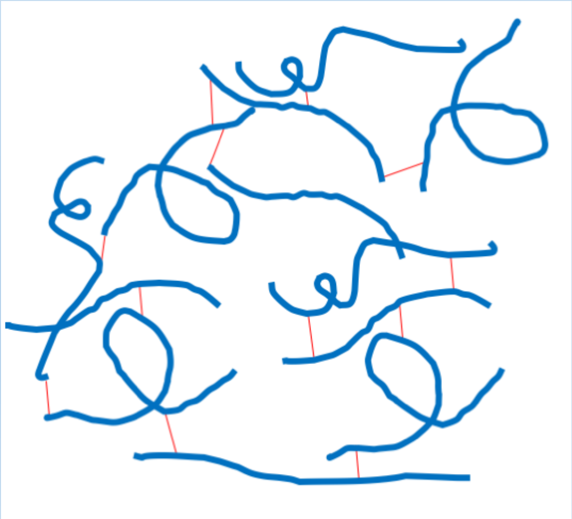


Determine biomaterial types

- Natural biomaterials:
  - Collagen
  - Elastin

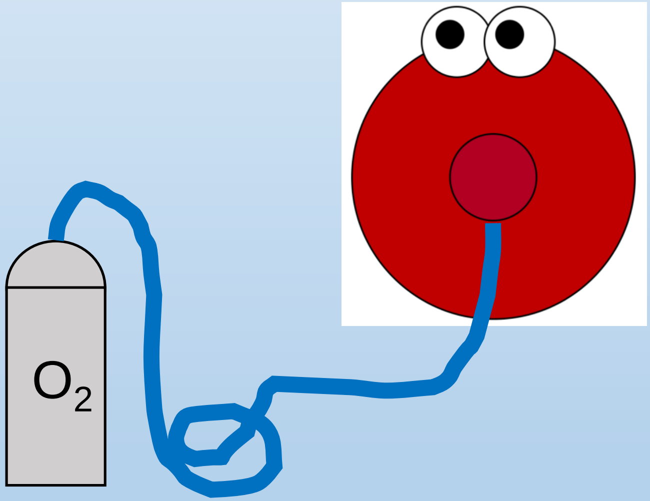


- Synthetic biomaterials:
  - “Polys”



Cell survival during printing

Image 12

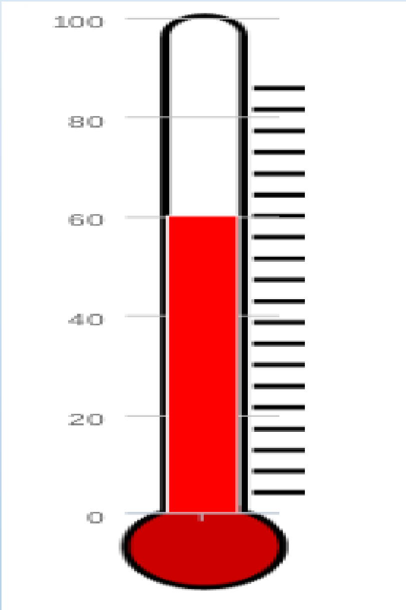


oxygen

Image 13

nutrients

Image 14



temperature

Applications of 3D bioprinting

- Current
  - Tissue mimics for drug testing and screening
  - Non-transplantable tissues and vessels

Image 15

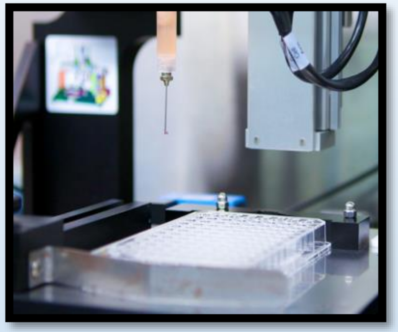
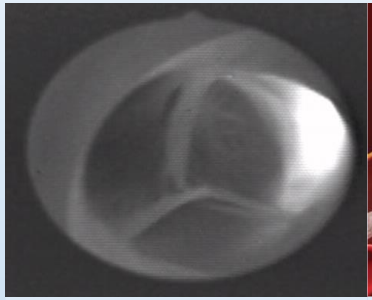
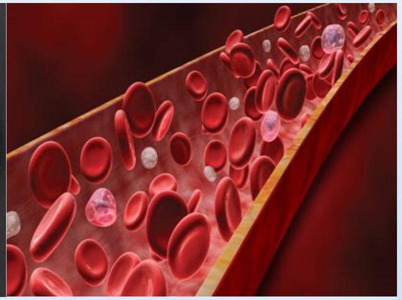


Image 16



aortic heart valve

Image 17



blood vessels

- Near future (~15 years)
  - Transplantable tissues

Image 18

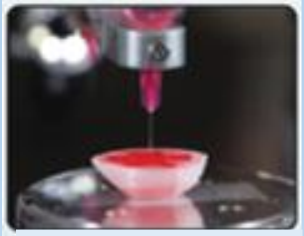
cartilage

Image 19

skin

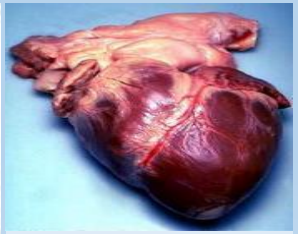
- Far future (~20+ years)
  - Organs

Image 20



kidney

Image 21



heart

Applications

Watch this video

Limitations

- Vascularization
- Immune rejection
- Biocompatibility

Image 22

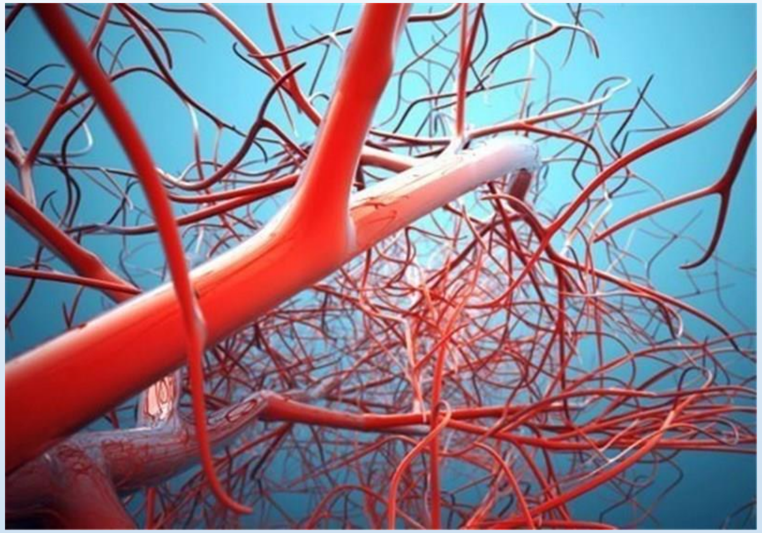


Image 23

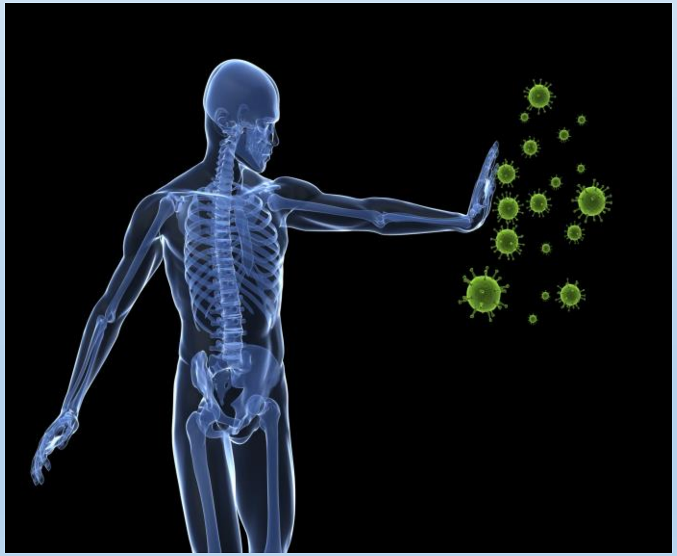
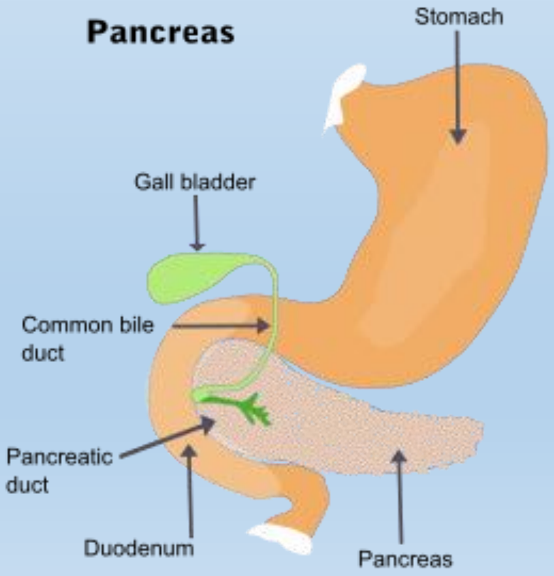


Image 24



Lesson Goals: Summary

- Introduce engineering problem ("Bill")
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Activity Instructions

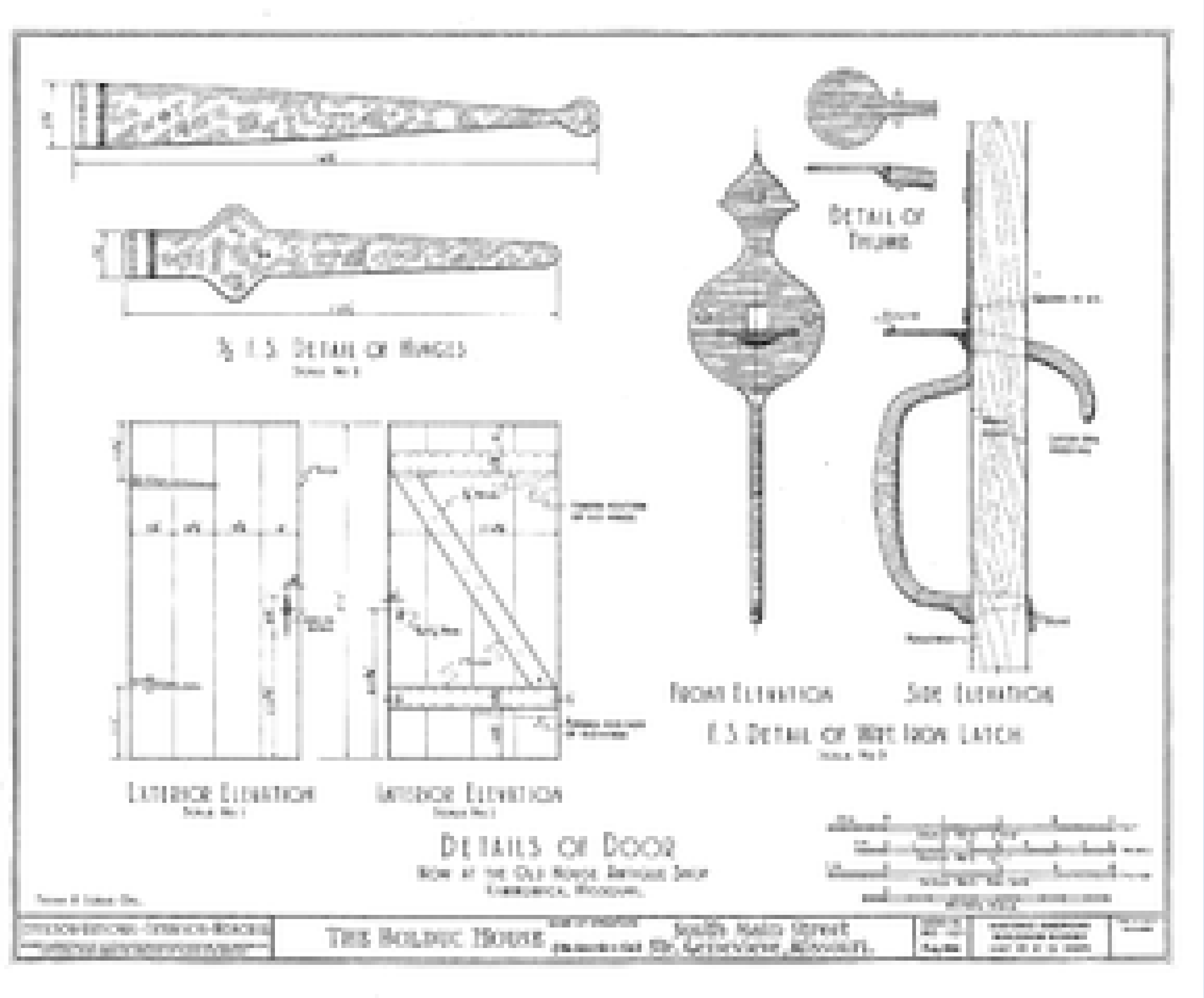
1. Review your assignments (~5 min)
2. Learn to use your mock bioprinter (~2 min)
3. Engineering sketch of your plan > ***get approval*** (~10 min)
4. Get biomaterials and print! (~20 min)
5. Present your design and limitations (~2 min for each group)

Mock 3D Bioprinter Instructions for Use

Show this video

Engineering Sketch

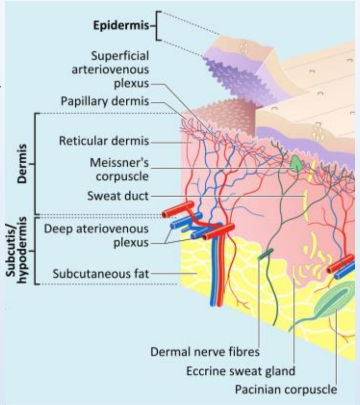
Image 25



- Diagram with labels
- Measurements and scale
- Axes, for reference

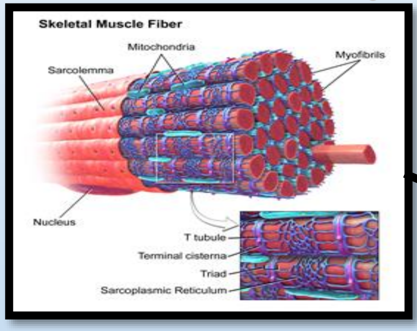
Bill's Injuries

Image 1



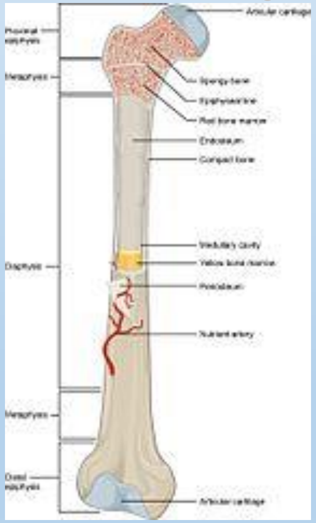
Missing skin on the left arm

Image 2



Ripped rectus femoral muscle

Image 3



Severely broken femoral shaft

Image Source/Rights

Image 1: Skin anatomy diagram | **File name**: skin1.jpg
Source/Rights: 2013 Anatomy Box, Creative Commons Attribution Share License http://www.anatomybox.com/chapters/skin/
Caption: An example of a skin tissue. Bill has injured skin.

Image 2: Muscle anatomy diagram | **File name**: muscle.jpg
Source/Rights: WikiJournal of Medicine Gallery of **Blausen** Medical, **2014.** CC Licensure 3.0. http://teachmeanatomy.info/the-basics/ultrastructure/histology-muscle/
Caption: An example of a muscle. Bill has a ripped femoral muscle.

Image 3: Anatomy of a long bone | **Image file name**: bone.jpg
Source/Rights: 2016 Carl Fredrick, Wikimedia Commons CC BY-SA 4.0 https://commons.wikimedia.org/wiki/File:603_Anatomy_of_a_Long_Bone.jpg
Caption: An example of a bone and underlying tissue. Bill has a broken femoral shaft.

Image 4: Uncle Sam saying "I want you to learn about 3D bioprinting." | **Image file name**: unclesam.jpg
Source/Rights: 2011 Library of Congress (public domain) https://www.loc.gov/exhibits/treasures/trm015.html AND https://www.loc.gov/item/93509735/
Caption: Some U.S. scientific research funding is going towards 3D bioprinting research.

Image 5: A photograph shows a 3D bioprinter with 4 extrusion heads | **Image file name**: regenhu.jpg
Source/Rights: 2016 RegenHu. All rights reserved. Used with Permission. http://www.aniwaa.com/product/3d-printers/regenhu-3ddiscovery/

Image 6: A photograph shows a 3D bioprinted tissue being taken out of growing media. | **Image file name**: tissue.jpg
Source/Rights: 2016 Anderson, Ojada, Nguyen. Governor's School of Architecture. All rights reserved. Used with permission. https://govschoolagriculture.com/tag/3d-bioprinting/
Caption: A 3D bioprinted tissue that is kept in media to allow cells to grow.

Image 7: A photograph shows of 3D bioprinted structure in the shape of an ear. | **Image file name**: ear.jpg
Source/Rights: Wake Forest Institute for Regenerative Medicine. Non-published. Used with permission. http://www.wakehealth.edu/WFIRM/
Caption: 3D bioprinters can build structures that are in the shape of an ear.

Image 8: Diagram shows a model of an inkjet bioprinter. | **Image file name**: inkjet.jpg
Source/Rights: 2016 Arslan-Yildiz, Assal, Chen, Guven, Inci, Demirci. Used with permission. http://iopscience.iop.org/article/10.1088/1758-5090/8/1/014103
Caption: Inkjet bioprinters disperse cells over a surface covering much area quickly.

Image Source/Rights

Image 9: A diagram of a laser-assisted 3D bioprinter. | **Image file name**: laser.jpg
Source/Rights: 2016 Arslan-Yildiz, Assal, Chen, Guven, Inci, Demirci. Used with permission. http://iopscience.iop.org/article/10.1088/1758-5090/8/1/014103
Caption: A laser-assisted bioprinter use lasers to force cells onto specific locations of the printing surface.

Image 10: A diagram of an extrusion 3D bioprinter. | **Image file name**: extrusion.jpg
Source/Rights: 2016 Arslan-Yildiz, Assal, Chen, Guven, Inci, Demirci. Used with permission. http://iopscience.iop.org/article/10.1088/1758-5090/8/1/014103
Caption: Extrusion bioprinters extrude cells within a filament. The filament/cell mixture forms the structure we see.

Image 11: A photograph of a 3D bioprinter with 2 extrusion heads printing onto a cell culture plate called a 96-well plate. | **Image file name**: organovo.jpg
Source/Rights: 2016 Organovo. Used with Permission http://www.csmonitor.com/Technology/2015/0519/3D-printing-human-skin-The-end-of-animal-testing
Caption: Extrusion 3D bioprinters have multiple heads to print from. They can also print on different surface. A computer system controls the rate of extrusion, the location, and which material is extruded.

Image 12: A graphic of a cell having oxygen delivered to it. | **Image file name**: oxygen.jpg
Source/Rights: 2017 Nick Asby (author), UVa Department of Biomedical Engineering. **Caption**: Cells need proper oxygen concentrations to survive.

Image 13: A picture of bottle of cell media | **Image file name**: media.jpg
Source/Rights: 2011 Lillly_M, Max Planck Institute for Molecular Cell Biology and Genetics in Dresden, Wikimedia Commons CC BY-SA 3.0
https://commons.wikimedia.org/wiki/File:Glasgow_MEM_cell_culture_medium.jpg
Caption: Cells are kept in cell media while they grow. Media provides nutrients, proper pH, water, and other compounds need to make cells grow.

Image 14: A graphic of a thermometer | **Image file name**: temperature.jpg
Source/Rights: 2004 Microsoft Corporation, One Microsoft Way, Redmond, WA 98052-6399 USA. All rights reserved
Caption: Cells need to be kept at proper temperatures to replicate and survive.

Image 15: A picture of 3D bioprinter printing into a cell culture container. The one in this picture is called a 96-well plate. | **Image file name**: drugTest.jpg
Source/Rights: 2016 Organovo. Used with permission. http://www.csmonitor.com/Technology/2015/0519/3D-printing-human-skin-The-end-of-animal-testing
Caption: 3D bioprinters are utilized by companies and researchers to create testing tissue for pharmaceutical research.

Image 16: A still image taken from an animation/video of beating bioprinted aortic valve. | **Image file name**: valve.gif
Source/Rights: 1989 Valveguru, Wikimedia Commons CC BY-SA 3.0 https://commons.wikimedia.org/wiki/File:Aortic_valve.gif
Caption: Researchers use 3D bioprinters to create valves. These are used for research purposes and cannot be placed in humans yet.
Original caption: This is still image pulled from a video clip of a living, beating pig heart—an aortic valve—that was bioprinted in a lab. The heart was arrested, connected to the perfusion system and restarted. The working fluid was oxygenated balanced saline solution.

Image Source/Rights

Image 17: A picture of cells laid down to create a blood vessel. | **Image file name**: vessel.jpg
Source/Rights: 2004 Microsoft Corporation, One Microsoft Way, Redmond, WA 98052-6399 USA. All rights reserved
Caption: Scientists have methods of creating blood vessels with 3D bioprinting methods.

Image 18: A picture of bioprinted cartilage in the shape of an ear. | **Image file name**: cartilage.jpg
Source/Rights: Wake Forest Institute for Regenerative Medicine. Non-published. Used with permission. http://www.wakehealth.edu/WFIRM/
Caption: Scientists can bioprint cartilage in the shape of an ear for research purposes. However, it is not safe to use these ears on humans.

Image 19: A picture of bioprinted skin being held. | **Image file name**: skin2.jpg
Source/Rights: Wake Forest Institute for Regenerative Medicine. Non-published. Used with permission. http://www.wakehealth.edu/WFIRM/
Caption: Scientists can print human skin for drug testing purposes. The skin does not have the exact structure of human skin, but it is a close replicate.

Image 20: A photo of a kidney being printed. | **Image file name**: kidney.jpg **Source/Rights**: Wake Forest Institute for Regenerative Medicine. All rights reserved. Non-published. Used with permission. https://govschoolagriculture.com/tag/3d-bioprinting/

Image 21: A picture of a human heart in vitro (outside the body) | **Image file name**: heart.jpg
Source/Rights: 2007 alexanderpiavas134, Wikimedia Commons (public domain) https://commons.wikimedia.org/wiki/File:Humhrt2.jpg
Caption: Scientists are working towards bioprinting hearts.

Image 22: A picture of a complex blood vessel system. | **Image file name**: vasculature.jpg
Source/Rights: 2004 Microsoft Corporation, One Microsoft Way, Redmond, WA 98052-6399 USA. All rights reserved
Caption: Incorporating blood vessel structure into tissues and organs requires complicated computer algorithms.

Image 23: A picture of a body rejecting pathogens. | **Image file name**: immune.jpg
Source/Rights: 2004 Microsoft Corporation, One Microsoft Way, Redmond, WA 98052-6399 USA. All rights reserved
Caption: Scientists are working to reduce of immune rejection when implanting a bioprinted tissue or organ into the body.

Image 24: A picture of pancreas attached to the gall bladder and bile duct. | **Image file name**: pancreas.jpg
Source/Rights: 2004 Microsoft Corporation, One Microsoft Way, Redmond, WA 98052-6399 USA. All rights reserved
Caption: Biocompatible bioprinted organs have the functionality, longevity, and mechanical properties that the original organ possessed.

Image 25: A multi-view engineering drawing | **Image file name**: engineeringSketch.png
Source/Rights: 1938 Frank R. Leslie, Historic American Engineering Record, National Park Service; Record MO-1105, Library of Congress, Prints & Photographs Division, MO-1105 (public domain) https://commons.wikimedia.org/w/index.php?curid=3715658
Caption: Engineering sketches include measurements, scales, dimensions and multiple views of the same design at different angles.