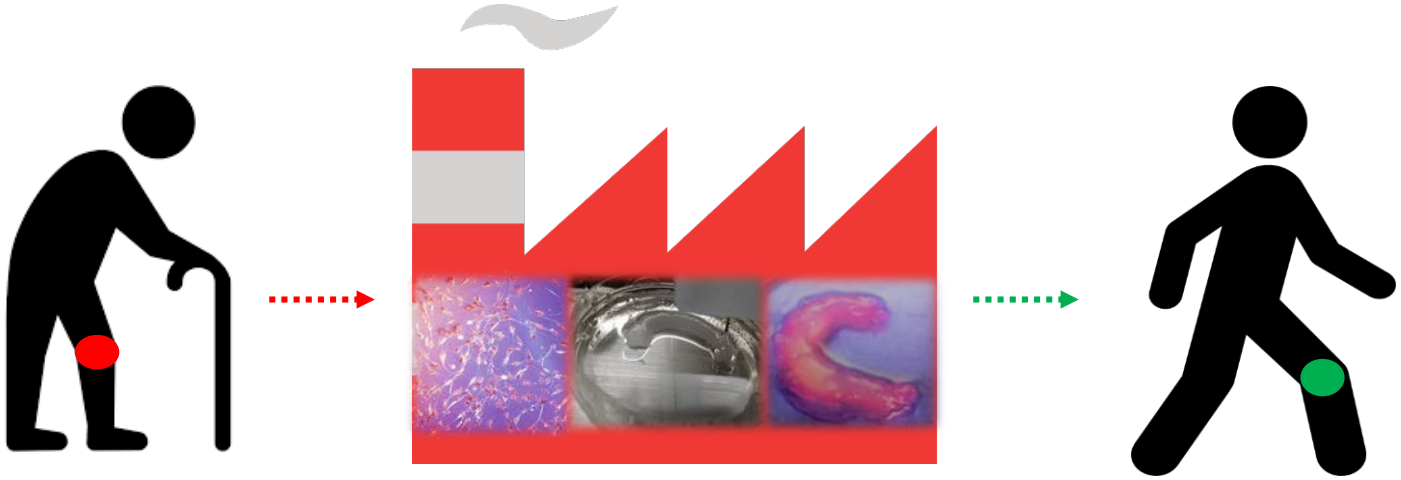
NC STATE UNIVERSITY

EDWARD P. FITTS DEPARTMENT OF INDUSTRIAL AND SYSTEMS ENGINEERING



Engineered Tissue "Factories"

to Enable Bench-to-Bedside Translation

Rohan Shirwaiker

Associate Professor, Industrial & Systems Engineering

Associate Faculty, Biomedical Engineering

Director, 3D Tissue Manufacturing Research Team

North Carolina State University

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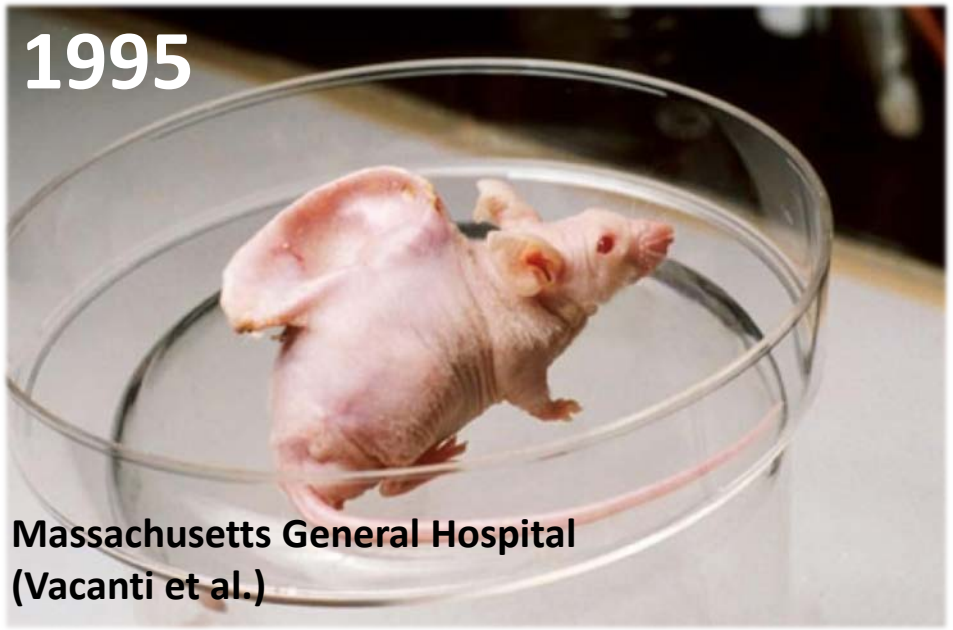
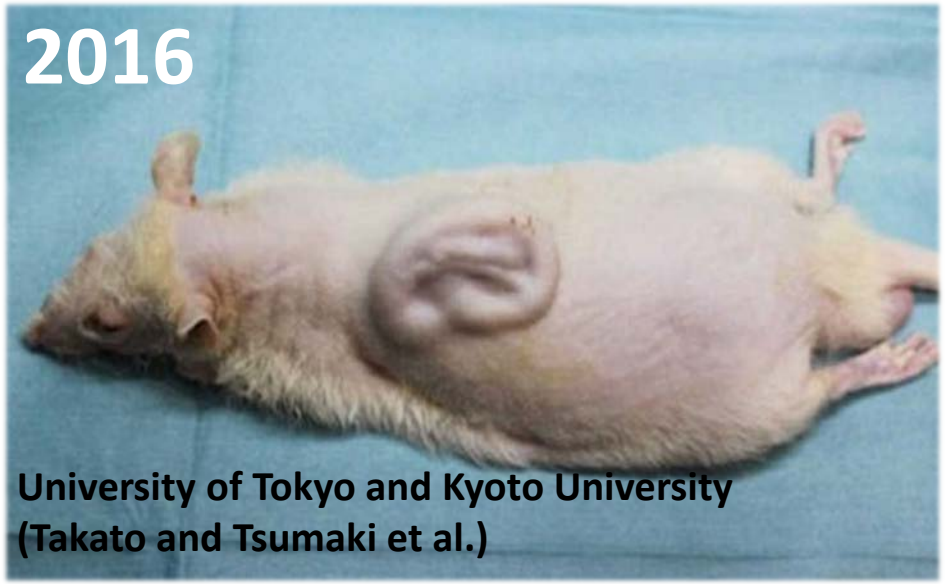
Tissue “Manufacturing”

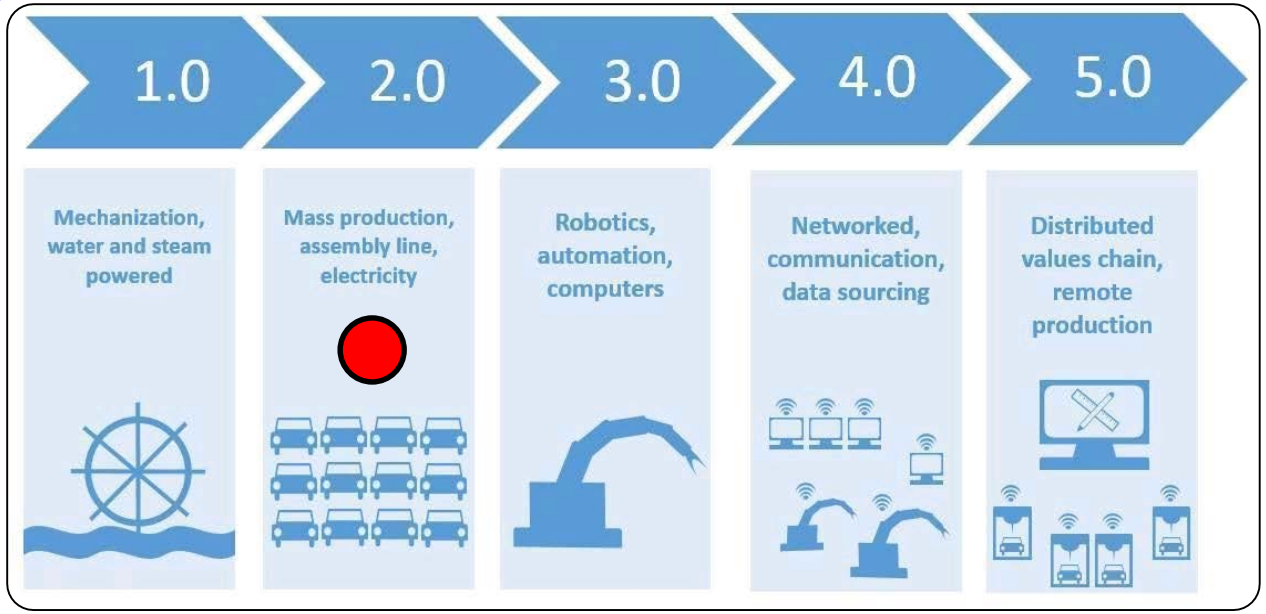


https://www.smithsonianmag.com/science-nature/history-lab-rat-scientific-triumphs-ethical-quandaries-180971533/

- Significant progress in relevant fundamental biomedical sciences not matched by advances in manufacturing science to enable scale-up and scale-out.
- Other industries are evolving towards Industry 5.0, but engineered tissue technology is still striving to make it to 2.0, for the most part.



https://www.medicaldaily.com/scientists-use-stem-cells-grow-human-ear-rats-back-371176



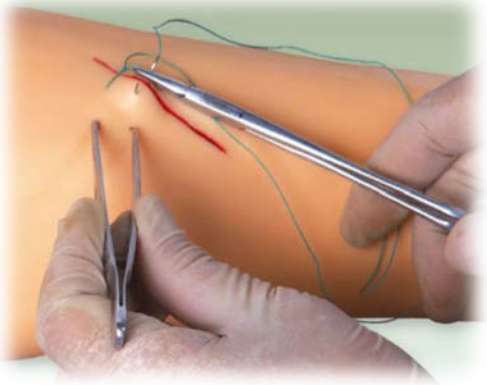
Engineered Tissues: Clinical Needs

Congenital Disorders

Trauma & Injuries

Chronic Diseases

Pharmaceuticals



Surgical Repair

Grafts & Transplants

Devices & Implants

Engineered Tissue Technology: Proofs of Concept

https://www.nature.com/articles/nbt.3413

https://iopscience.iop.org/article/10.1088/1758-5090/ab15cf

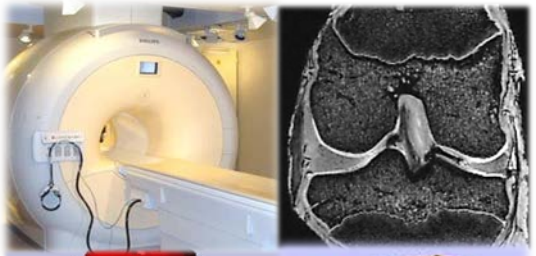
https://science.sciencemag.org/content/364/6439/458

Able to grow cells onto biomaterials…..

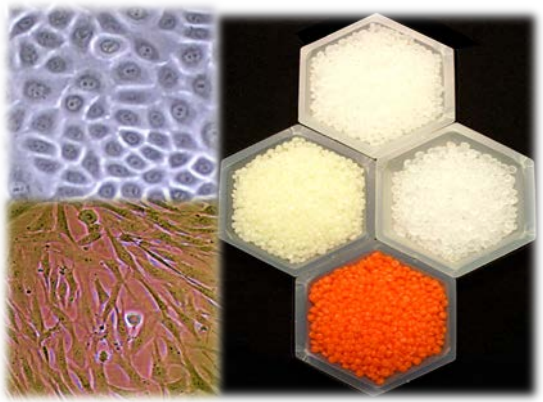
with tissue-specific characteristics…..

in patient-specific 3D geometries…..

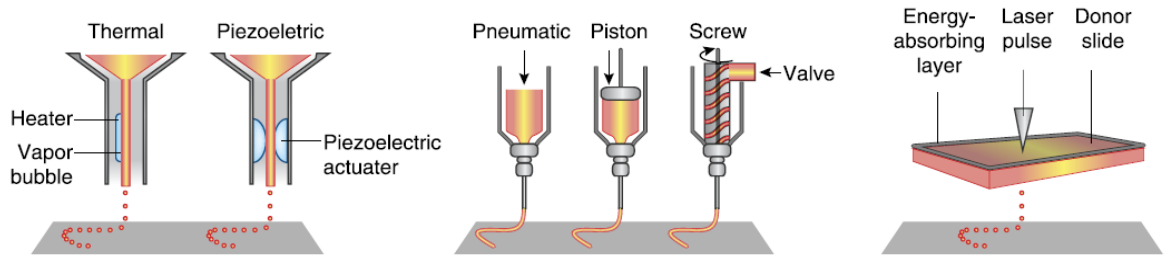
Current State of Tissue “Manufacturing”



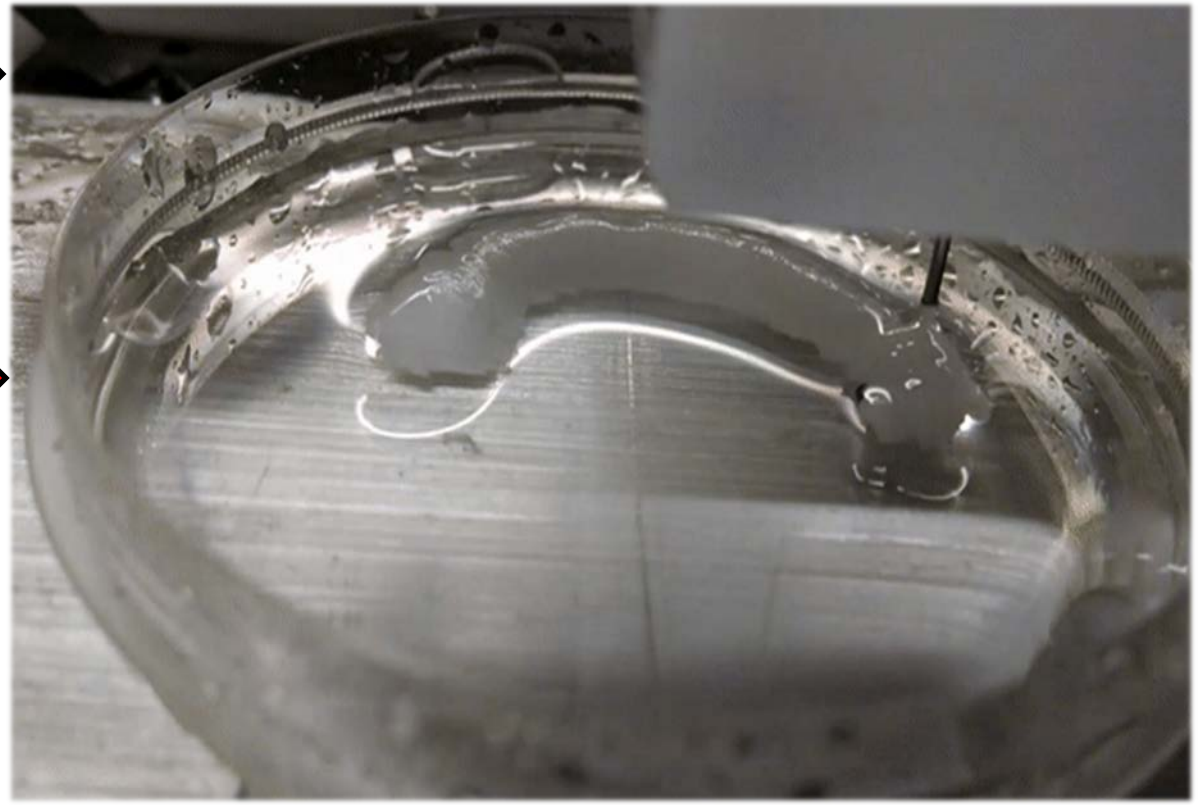
Biomodeling
(Imaging → CAD/CAM)



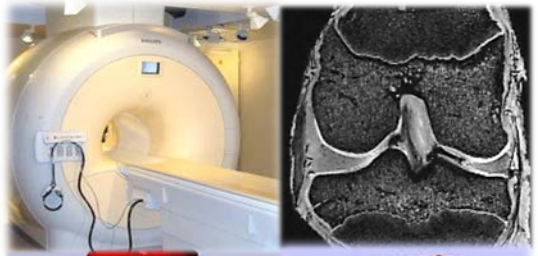
Bioinks
(Cells + Biomaterials)



Bioprinting Process Modalities



Current State of Tissue “Manufacturing”



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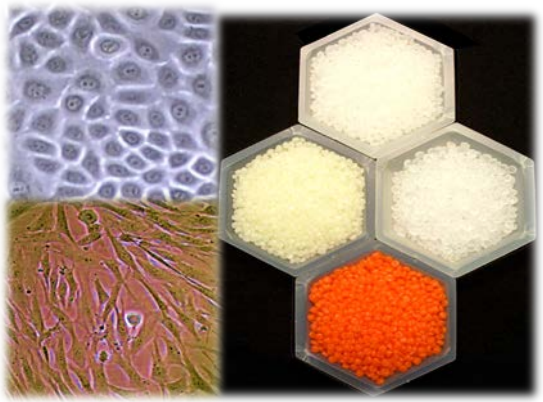
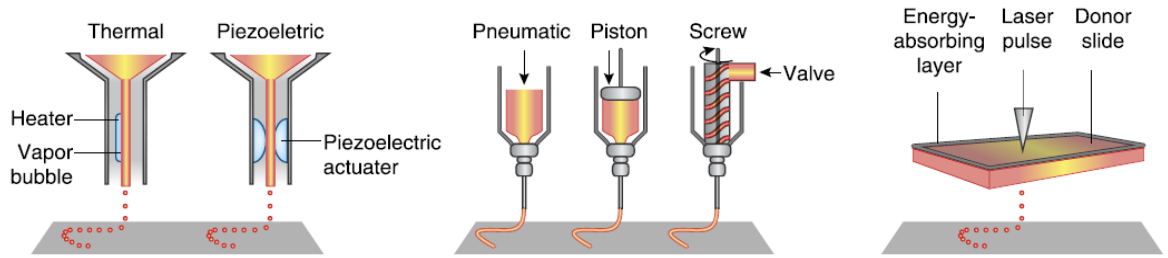


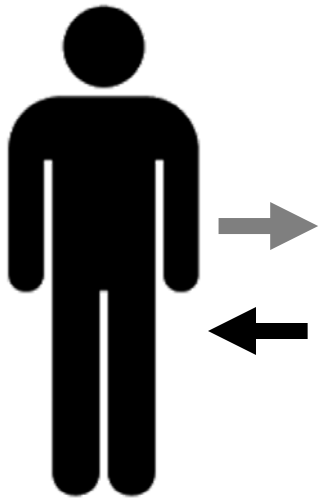
Bioinks
(Cells + Biomaterials)

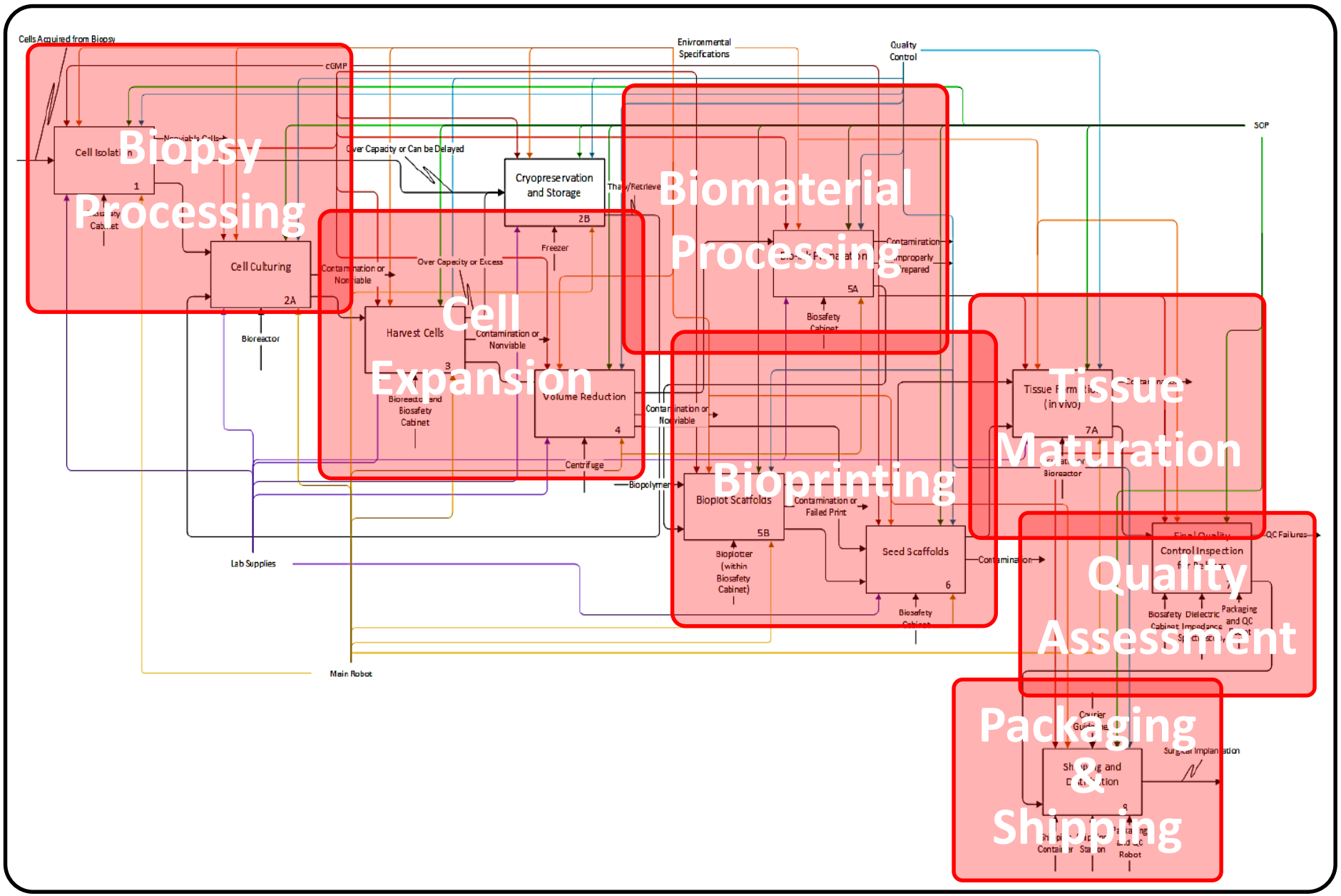


Bioprinting Process Modalities

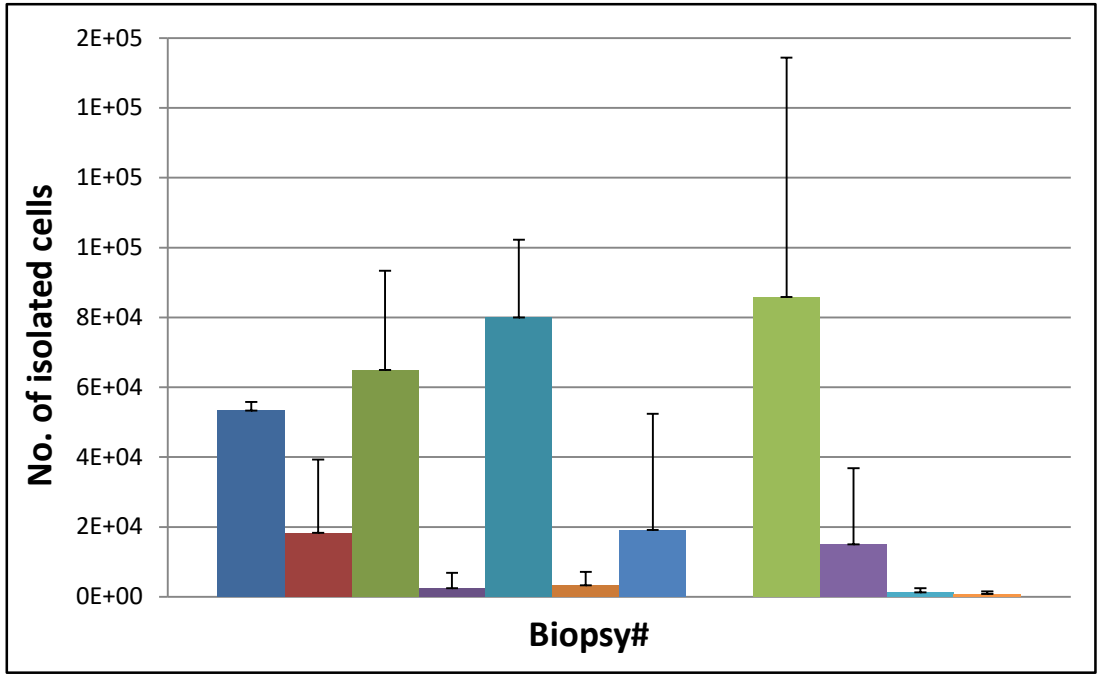
Bioprinting
≠
Tissue Manufacturing

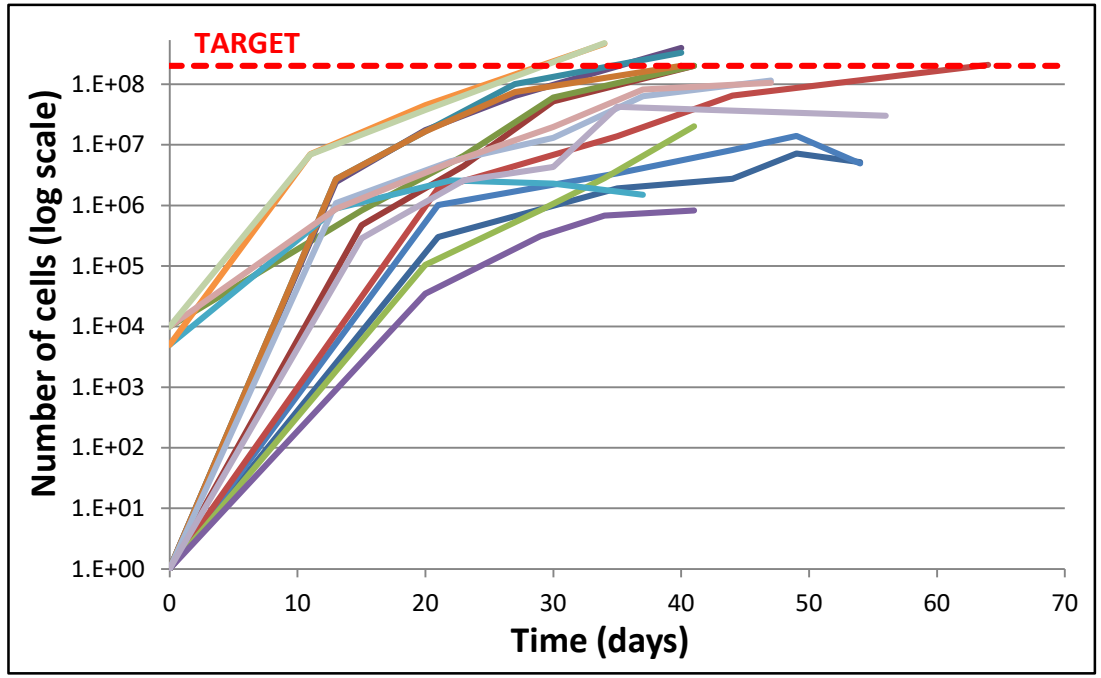
High-Level Map of Tissue “Manufacturing”





Example: Upstream Challenges



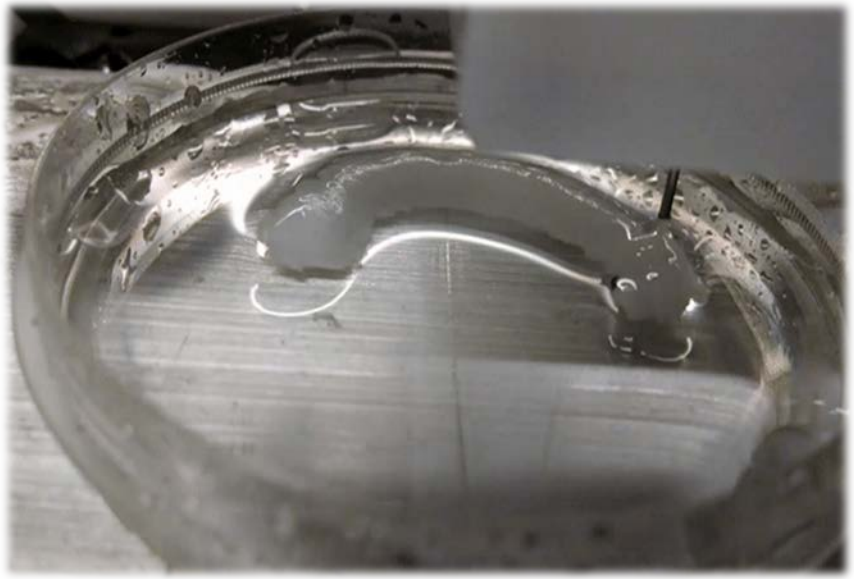


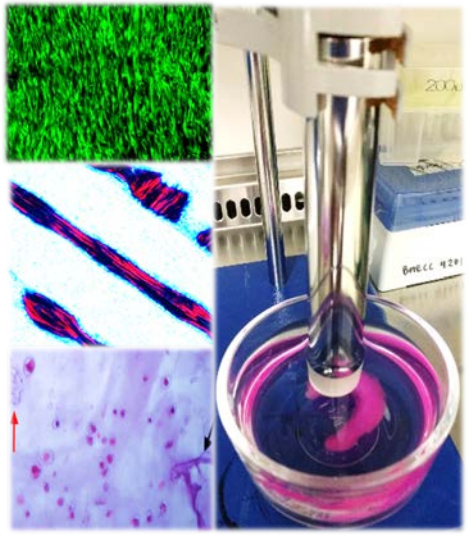
High upstream variability leads to more significant downstream disruptions (*bullwhip effect*)

⇒ Wasted resources

⇒ Scheduling issues in subsequent stages of bioprinting and implantation

Example: Downstream Challenges



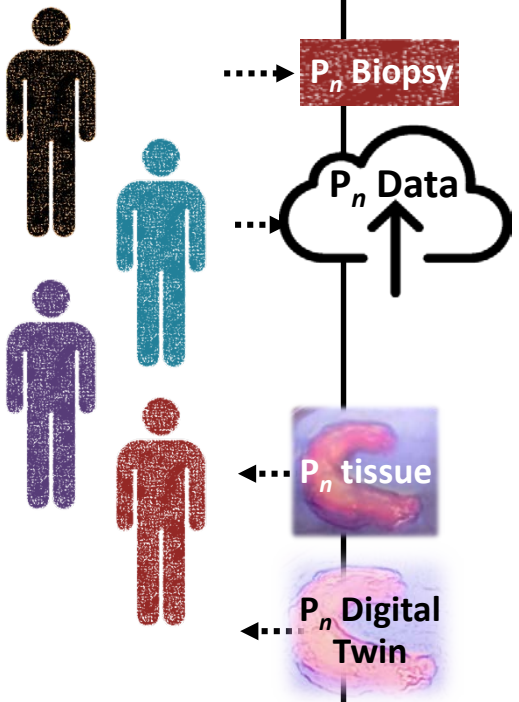


For quality inspection

For implantation

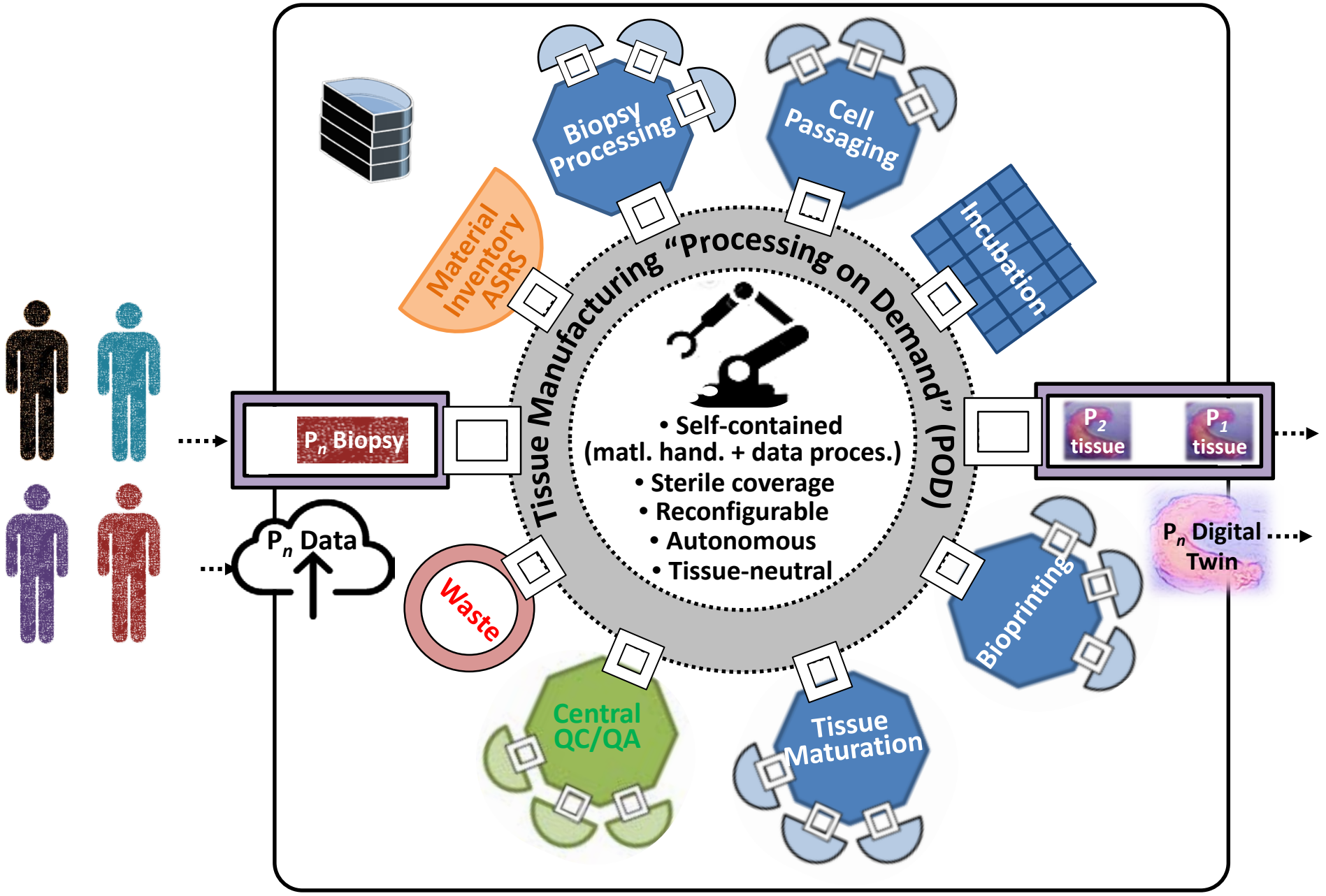
Vision for Tissue Manufacturing

Modular Scalable Smart Factories for Mass Production of Patient-specific Tissues at Point-of-Care

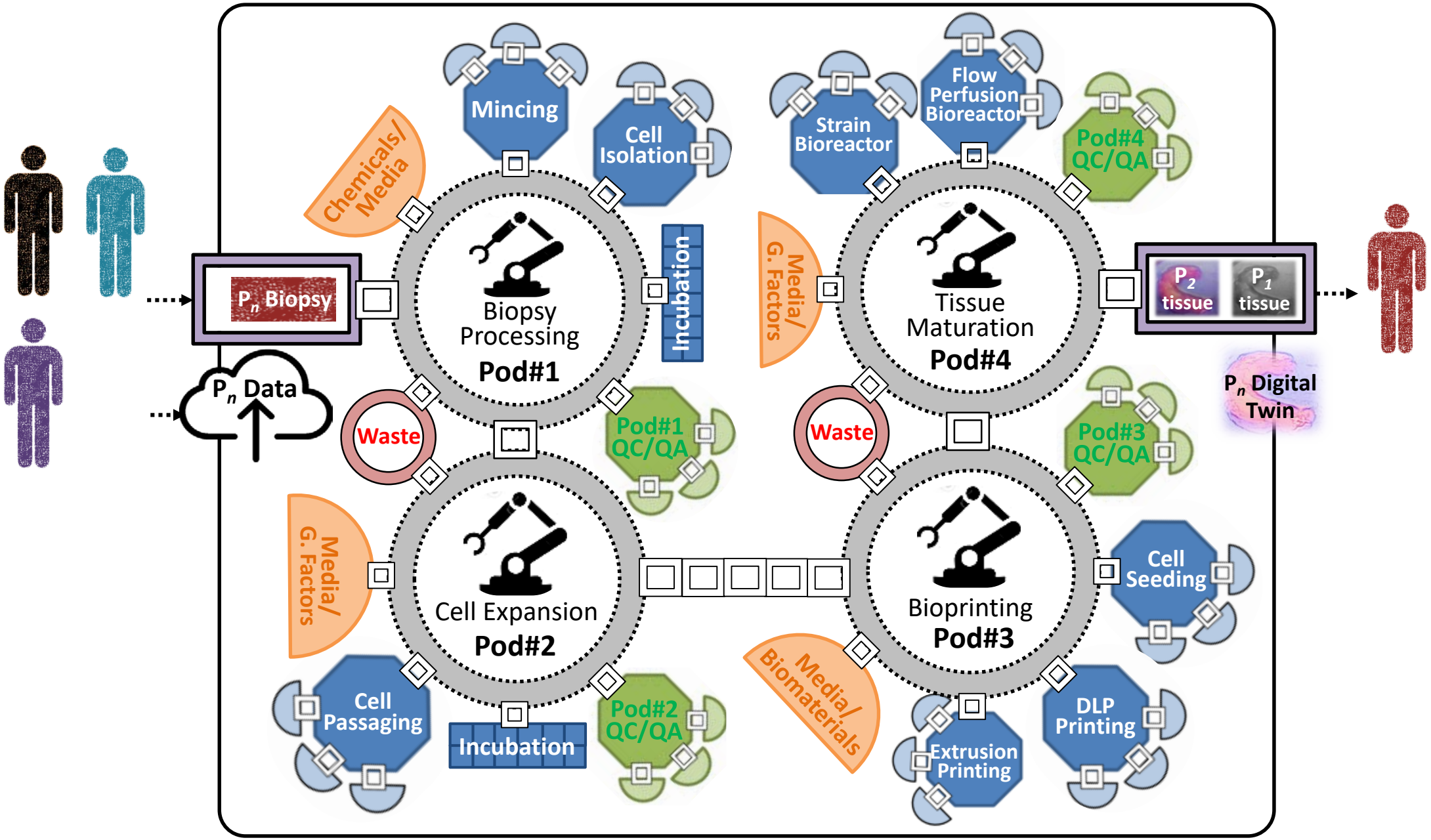


- Mass production with lot sizes of one
- End-to-end sterile environment with no cross-contamination between lots
- Stochastic processes with high variabilities (pre-dominantly biology driven)
- Process cycle times and production lead times spanning up to several weeks
- Transient properties of living raw material, WIP, and finished product leading to inventory constraints
- 100% inspection
- Continuous process improvement challenging due to regulations

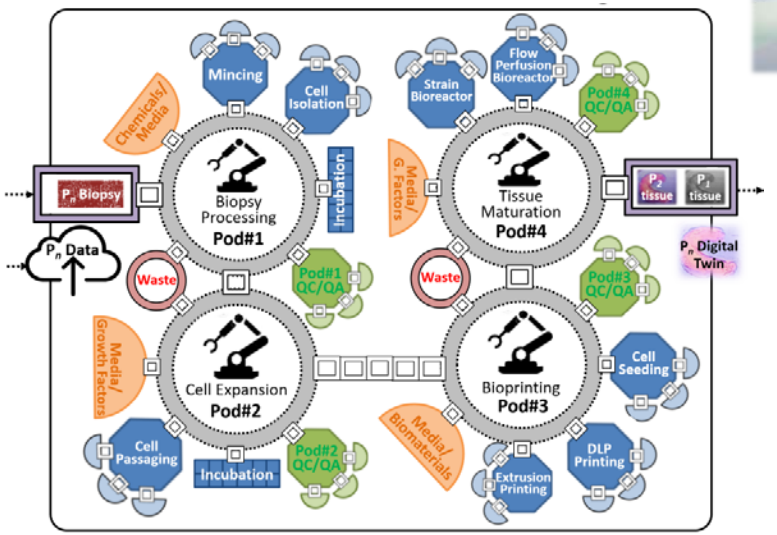
Vision for Tissue Manufacturing



Vision for Tissue Manufacturing



Vision for Tissue Manufacturing



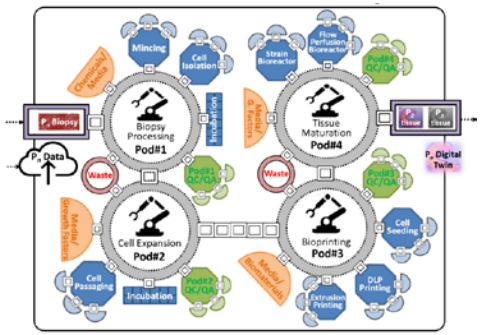
R&D of Critical Enablers

Education

Collaborations

- Cells
- Biomaterials

- Design for *X* (*Tissue Manufacturing, Implantability*)
- Process Design for Biomimicry
- Automation & Robotics
- Multi-variate Sensing



- Taxonomy & Ontology
- Cyber-physical System Architecture
- Machine Learning & AI
- Logistics & Supply Chain Design
- Data & Waste Management
- Economics & Decision-making Modeling

Regulations

Standards

Acknowledgements

Students, Collaborators & Mentors:

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- Dr. Jeffrey Spang
- Dr. Behnam Pourdeyhimi
- Dr. Anthony Atala

and others….