Applying Systems Thinking to Regenerative Medicine – A Workshop

October 22-23, 2020

SESSION V : Supply Chain and Cost Modeling

Novel Supply Chain and Process Modeling for Regenerative Medicine and Cell Therapy Manufacturing and Distribution

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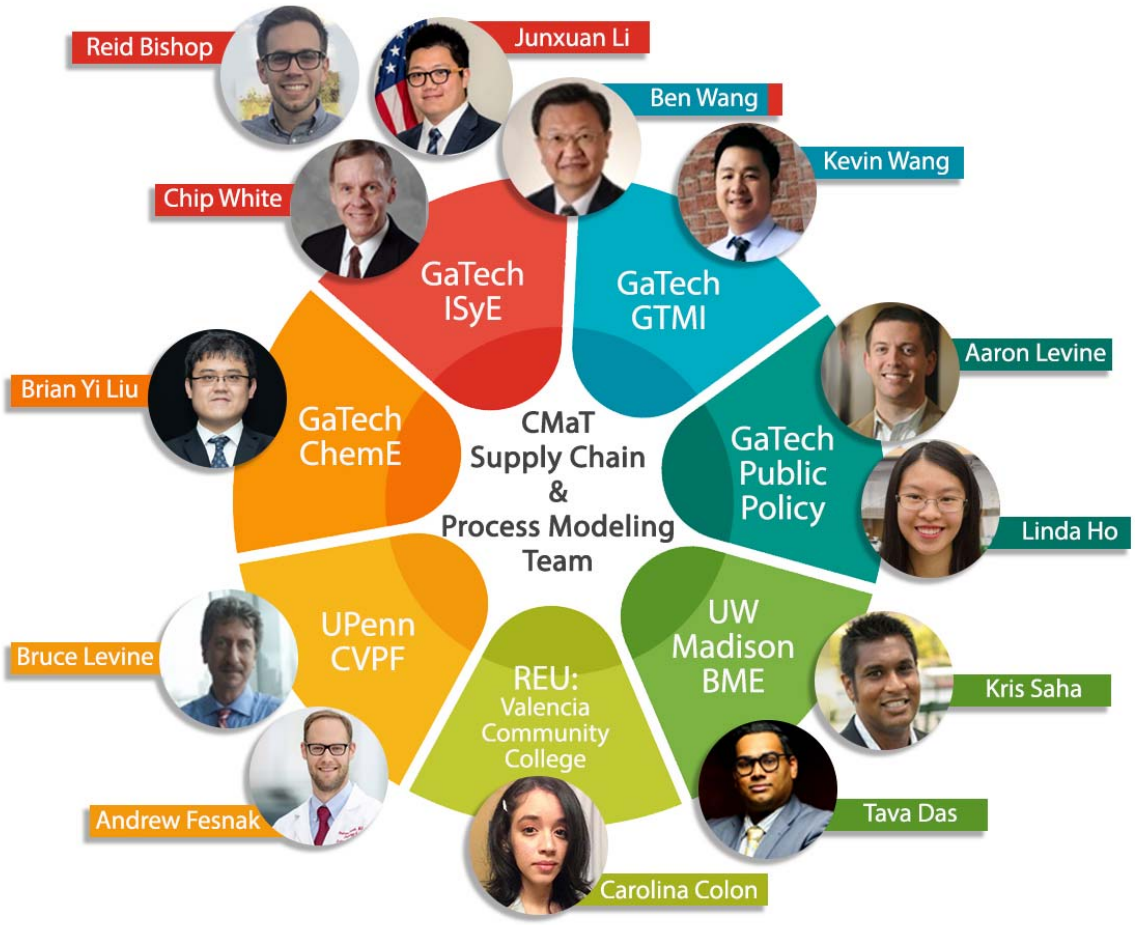
Novel Supply Chain and Process Modeling for Regenerative Medicine and Cell Therapy Manufacturing and Distribution



CMaT

Georgia Tech ISyE H. Milton Stewart School of Industrial and Systems Engineering

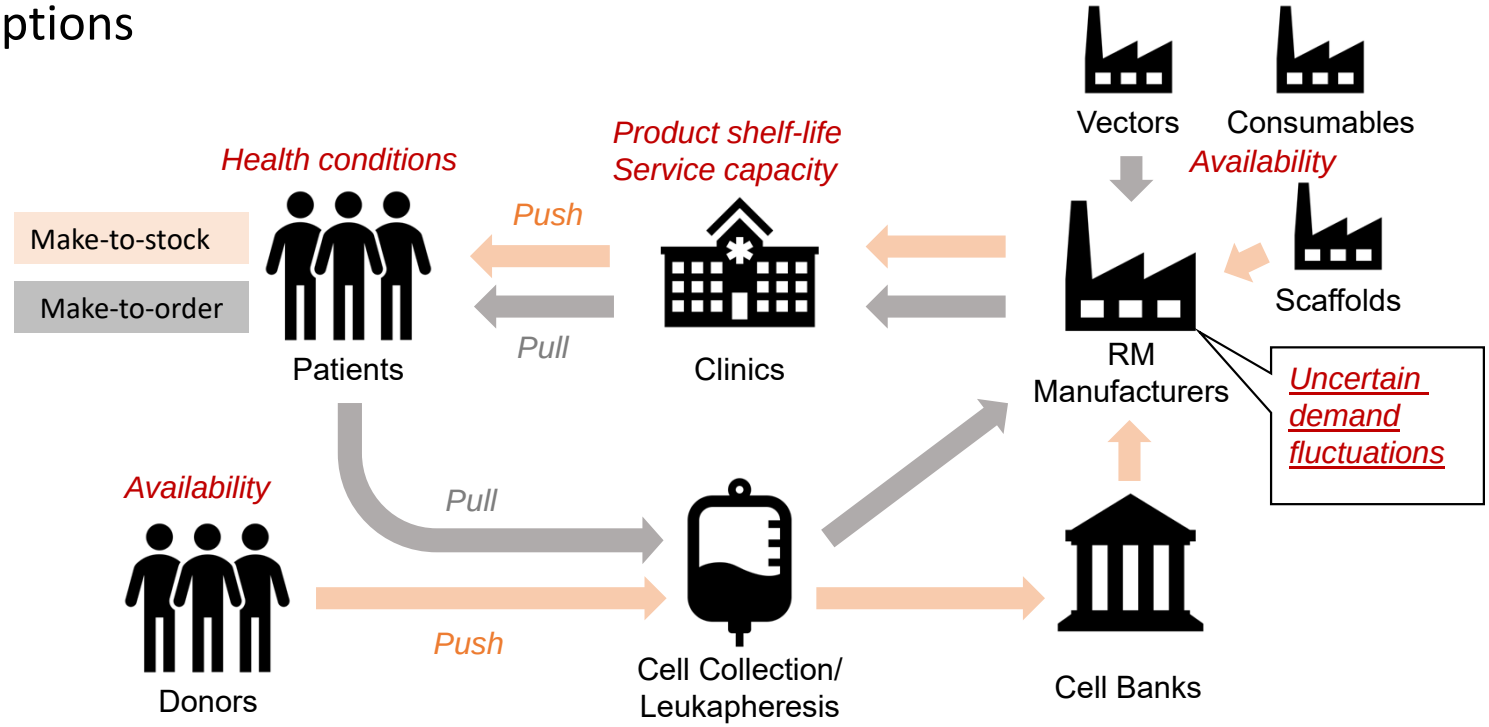
Georgia Tech Manufacturing Institute

Presentation Outline

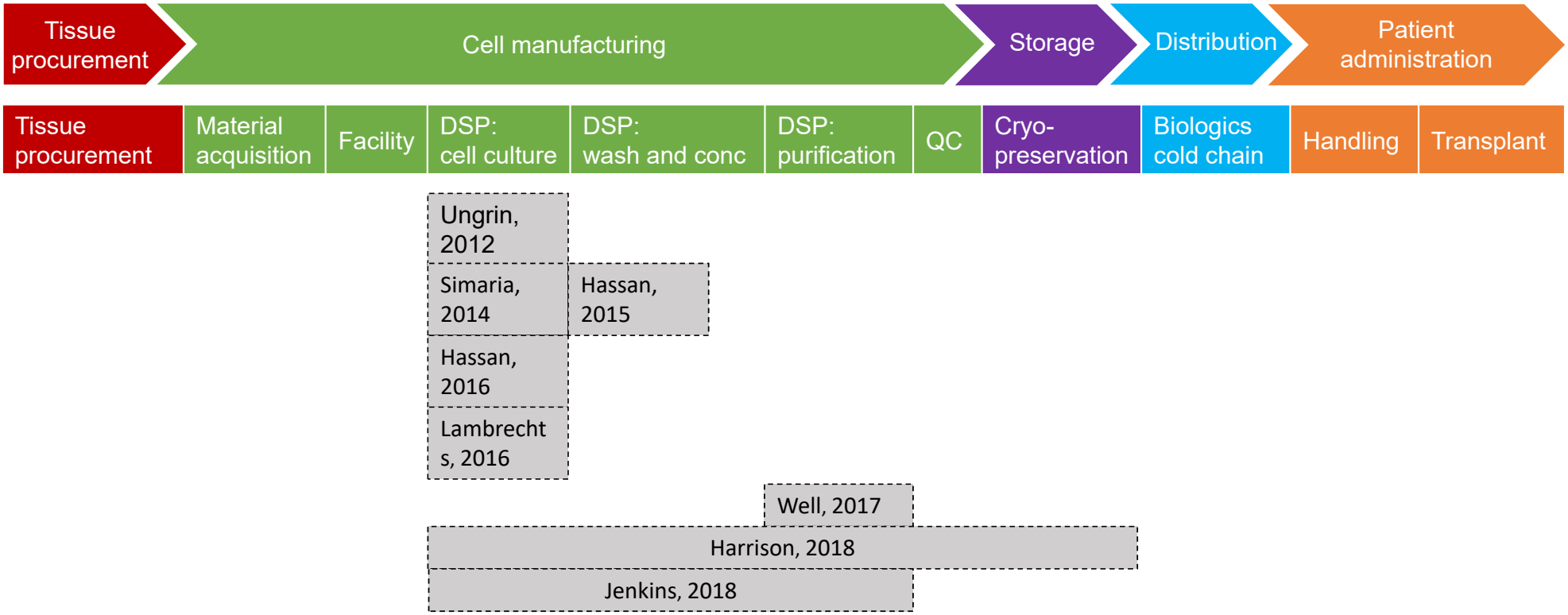
- On-going projects funded by NSF CMaT ERC and BioFabUSA
- Case studies: capacity planning, supply chain disruptions, demand surges & priority queue, cost of goods and automation

Challenges in Managing RM Supply Chains

- A large variety of products and complex supply chain issues (pull and push)
- Realtime impact of patient health conditions on production and supply chain planning
- Uncertainties including demand fluctuations, machine breakdowns, process failures, supply chain disruptions



Existing Digital Modeling Efforts

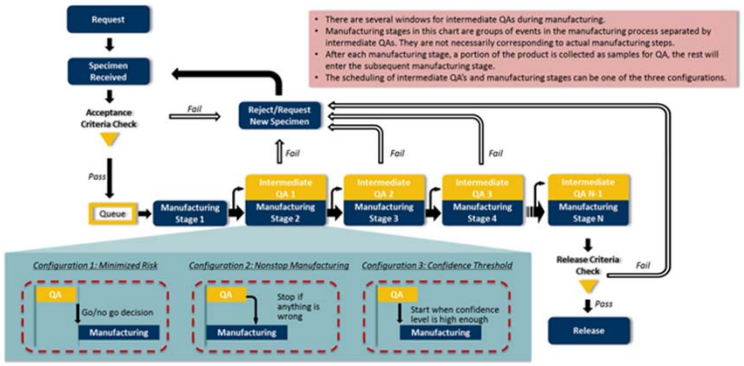


Lam, Ching, E. Meinert, A. Alturkistani, A. R. Carter, J. Karp, A. Yang, D. Brindley, and Z. Cui., "Decision Support Tools for Regenerative Medicine: Systematic Review," Journal of medical Internet research, Vol. 20, No. 12, e12448, 2018.

Project Objectives

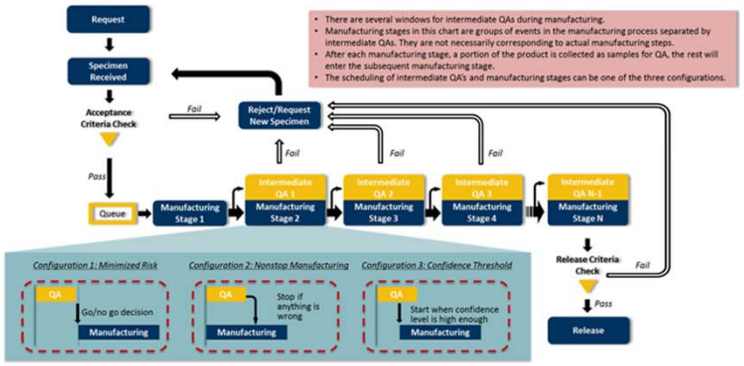
- Build a decision support toolset to incorporate all stakeholders' perspectives into supply chain system design, planning and control
- Develop and validate digital models (single production facility and a network of production facilities) of manufacture and quality assurance for regenerative medicine and cells to support reliable, scalable manufacturing of quality, affordable therapeutics
- Inform standards and regulation development
- Support and participate in education and workforce development

Two-Level Modeling Approach: One Production Facility



(a) Single facility production process and decision flow chart

Two-Level Modeling Approach: Network View



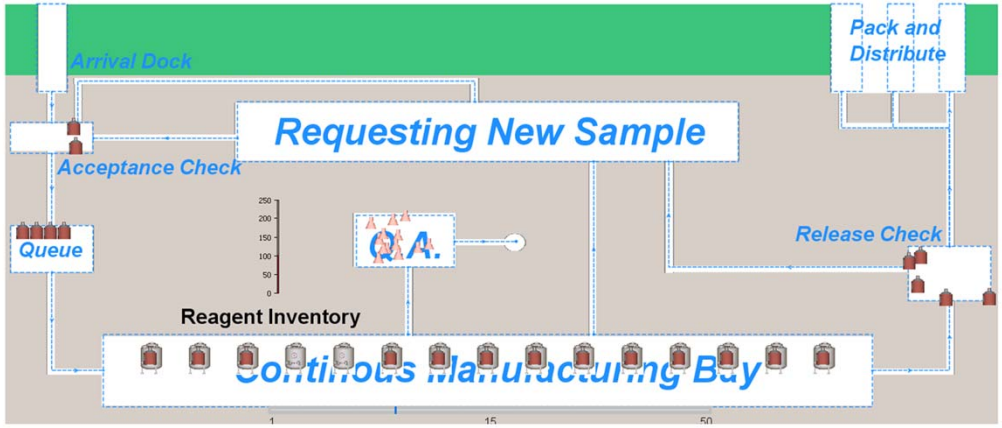
(a) Single facility production process and decision flow chart

(b) Centralized production model

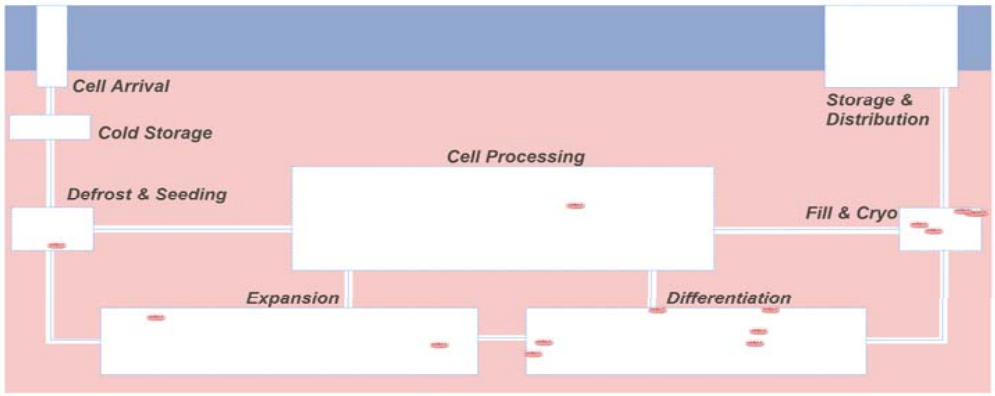
(c) Regional production hub model

(d) Point-of-care production model

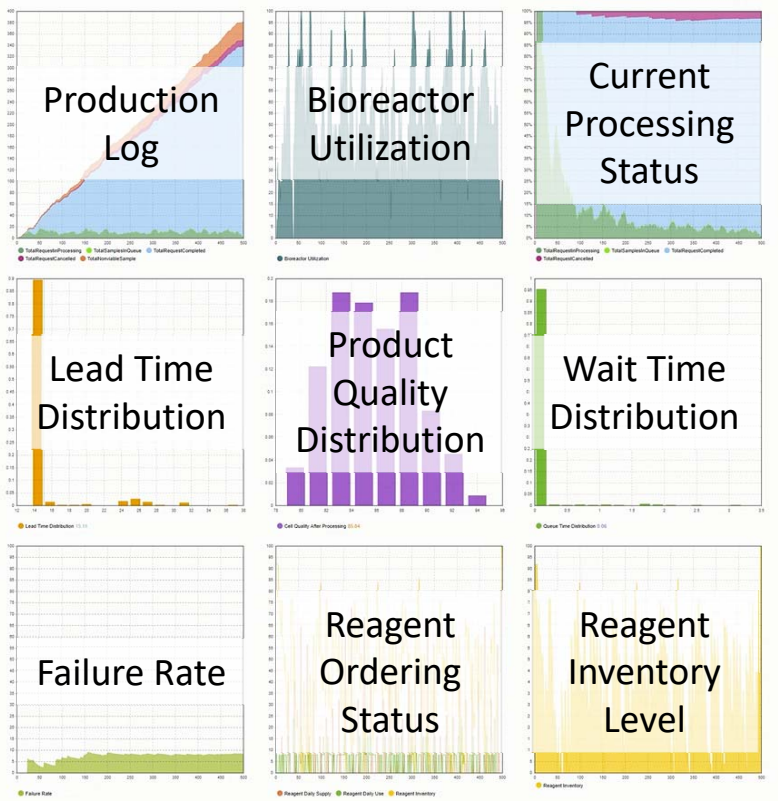
Digital Modeling & Simulation Provides a Wealth of Information



Autologous CAR-T facility Layout

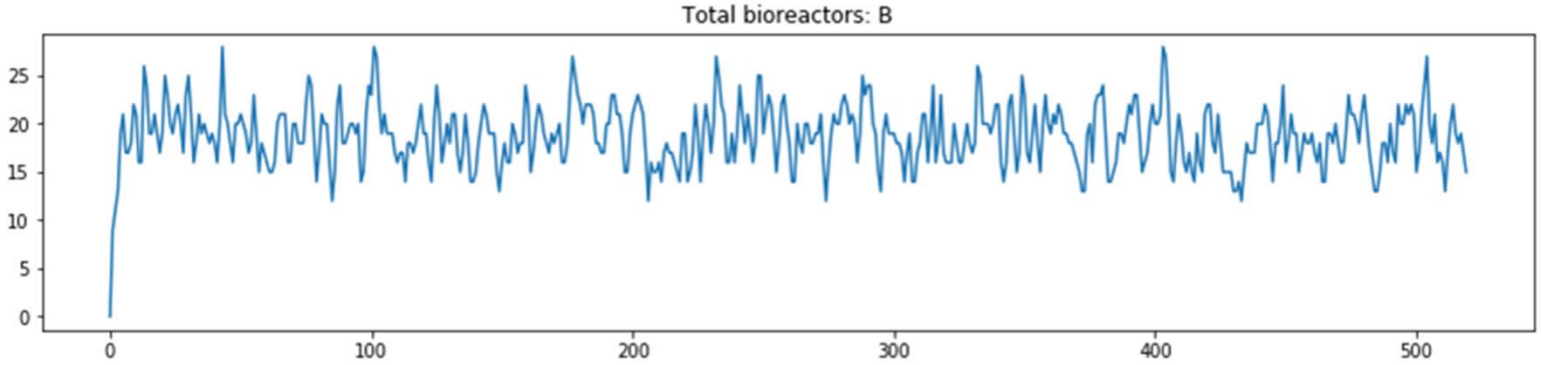


Allogeneic iPSC facility layout



Production Statistics

Production Capacity Planning

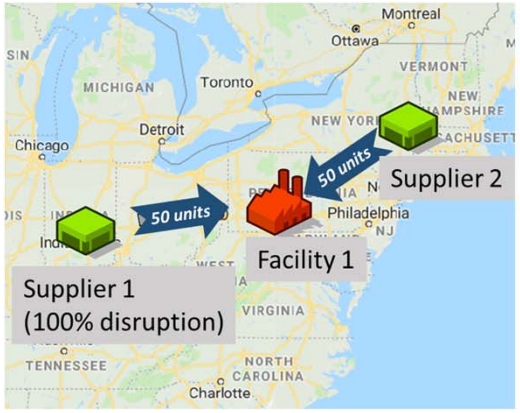


B	P(delay)	P(short in bioreactor)	P(short in reagent)
21	0.057	0.041	0.025
22	0.043	0.023	0.025
23	0.035	0.014	0.025

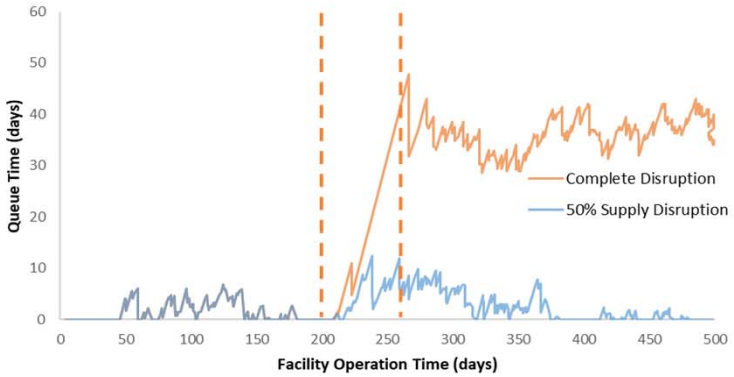
Risk-Mitigation Strategy Evaluation: Supplier Disruptions

Scenario

Multiple Supplier



Queue Time



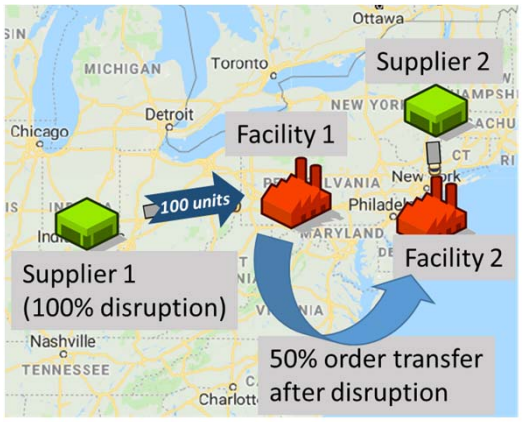
Effect

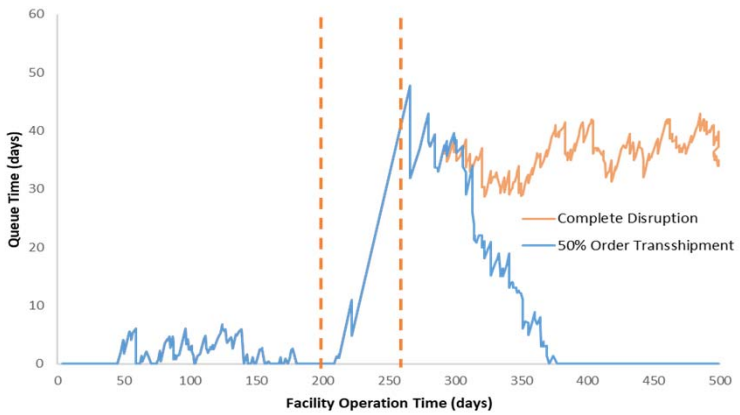
	1 Supplier 1 Facility	2 Suppliers 1 Facility
Time to restore the original steady state (Days)	∞	121
Average Queue Time Increased (Days)	28.5	2.9

Risk-Mitigation Strategy Evaluation: Supplier Disruptions

Scenario	Queue Time	Effect

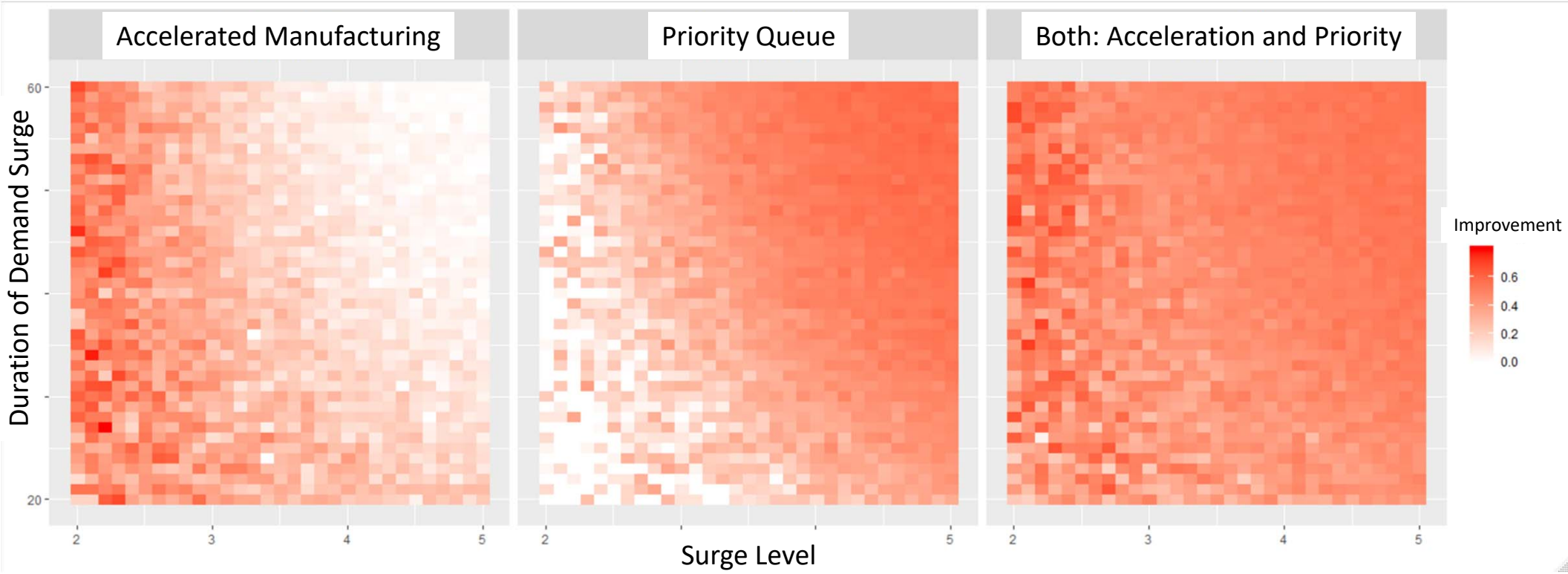
Order Transshipment





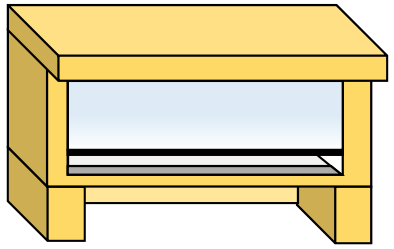
	1 Supplier 1 Facility	2 Suppliers 2 Facilities
Time to restore the original steady state (Days)	∞	117
Average Queue Time Increased (Days)	28.5	18.7

Policy Evaluations in Response to Demand Surges

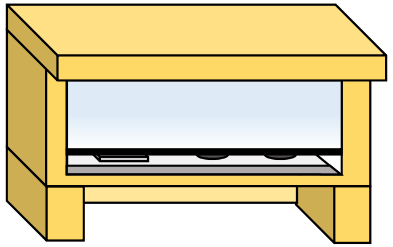


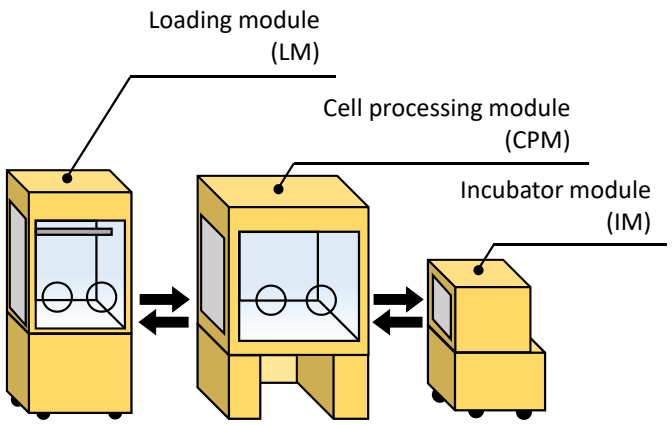
Automating Allogeneic iPSC Production & Cost Modeling

① Manual operation・
Biosafety cabinet (BSC)

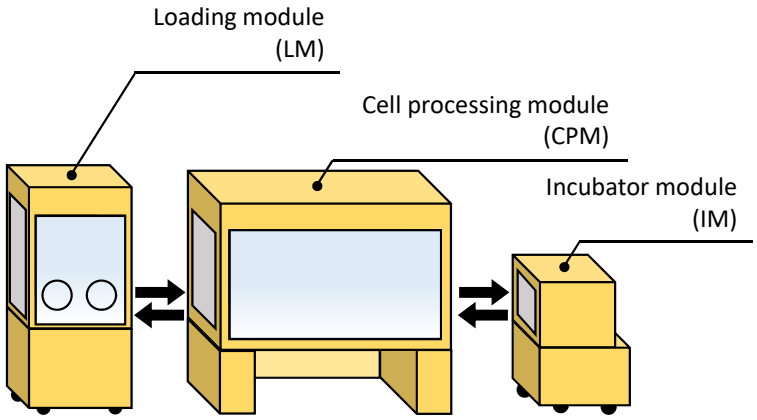


② Automatic operation・
Biosafety cabinet (BSC)





③ Manual operation・Isolator system (IS)



④ Automatic operation・Isolator system (IS)

Automation appears to show cost and throughput advantages

- Manual operations require much more labor leading to a lower throughput compared to automated systems
- Isolators are more expensive and more labor intensive than biosafety cabinet
- Automation with biosafety cabinets has the lowest unit cost whereas automation with isolators has the highest output

Configuration	Machine	Labor hour requirements per batch	Annual batches produced	Average cost per batch (USD)
Manual	Biosafety Cabinet	*125*	**21.7**	**$28.6k**
Automated	Biosafety Cabinet	*101*	**27.3**	**$18.4k**
Manual	Isolator	*173*	**15.3**	**$92.1k**
Automated	Isolator	*77*	**36.9**	**$27.6k**

- Factors yet to be considered: variability of cell quality and contamination risks
- All configurations are assumed operating under the same cleanroom conditions