Construction of a quantitative evaluation system for cell culture operation and cellular condition with a versatile humanoid robot

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Self-driving Cell Culture System

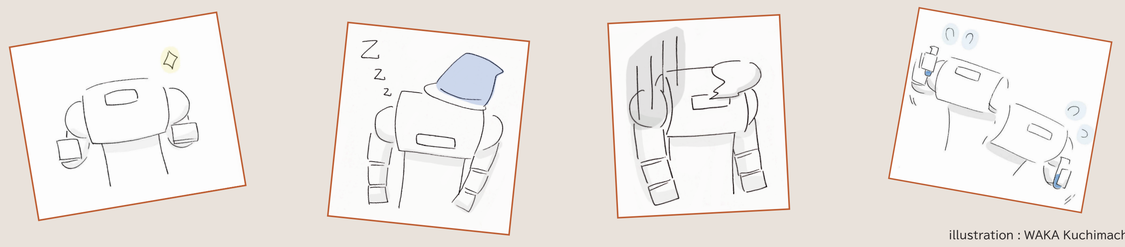
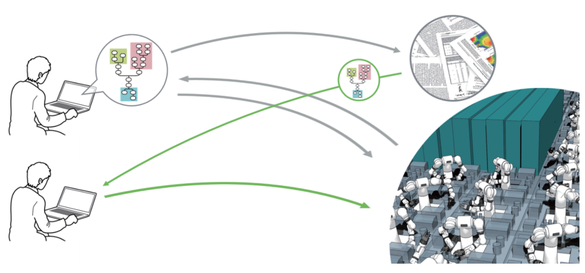


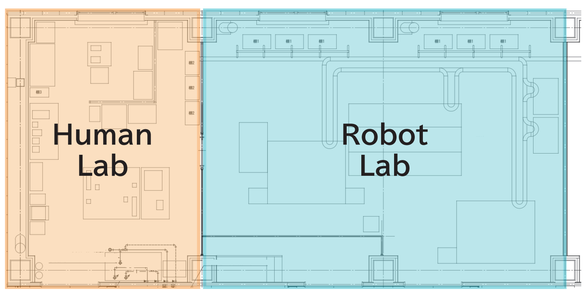
illustration : WAKA Kuchimachi

Our goal : Robotic Biology



Robotic biology center (RBC)

- Scientists send protocols to RBC
- Robots perform experiments
- Scientists receive the results
- all results are traceable
- all expriments are done at the same condition



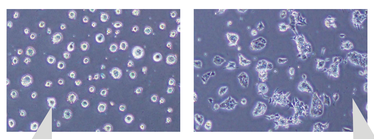
Prototyping Lab

- To try developed soft/hardware
- To do exemplary biological research
- To try combination of multiple robots of various manufactures
- To be a trial lab for external users
- To be used for education or demonstration

e.g. cell culture

The ”ambiguity” of human judgments and techniques reduces the accuracy and reproducibility of experiments.

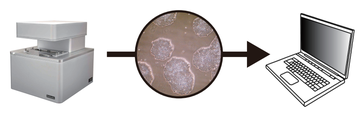
Evaluation issues



“It’s about time to passage”

“Somehow cells don’t look so good”

Non-quantitative decision criteria



cell evaluation without human eye

Technique issues



“Mix gently”

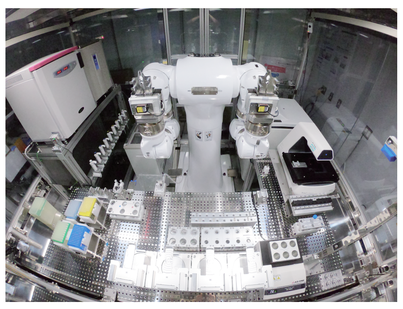
“Evenly seed cells”

Non-quantitative culture operation



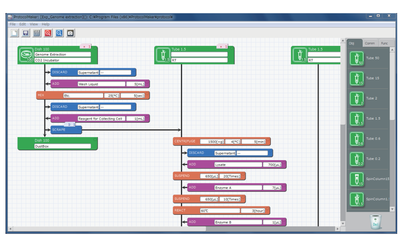
culture operation without human hand

versetile humanoid robot LabDroid Maholo



LabDroid Maholo

- 15 axis
- use the same machines and equipments as humans
- high reproducibility
- operation logging
- continuous 24-hour operation is possible

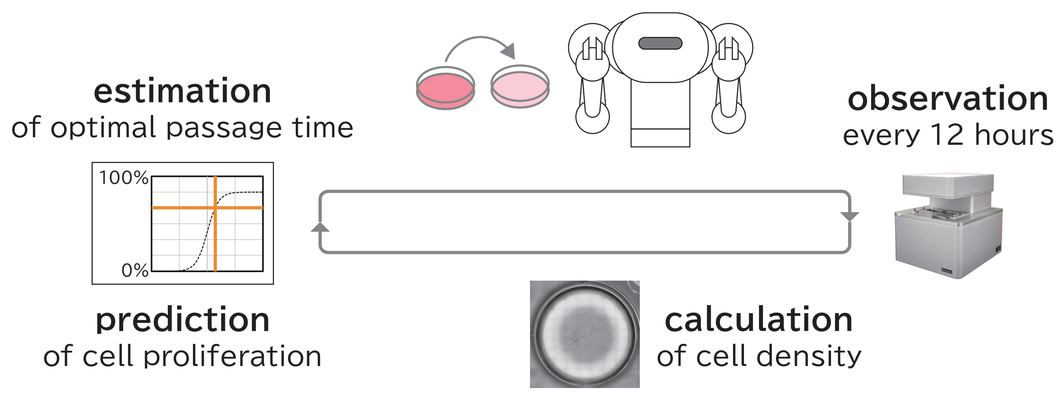


ProtocolMaker

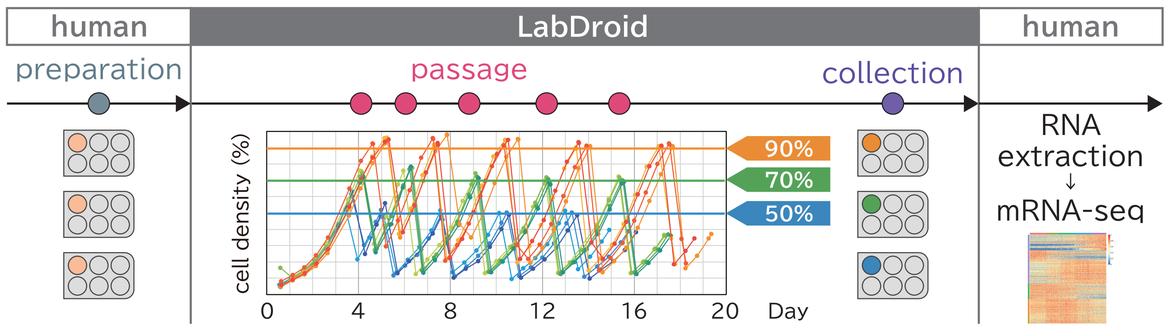
- users can make their own protocol simply by dragging and dropping
- No programming knowledge required
- made protocols are reusable by other Maholos

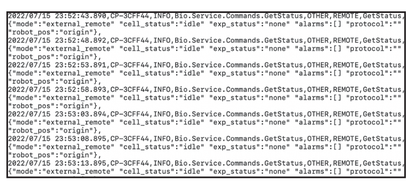
Autonomous cell passage

LabDroid passages cells based on predicted cell-proliferation by AI



cell culture with different cell densty at passage

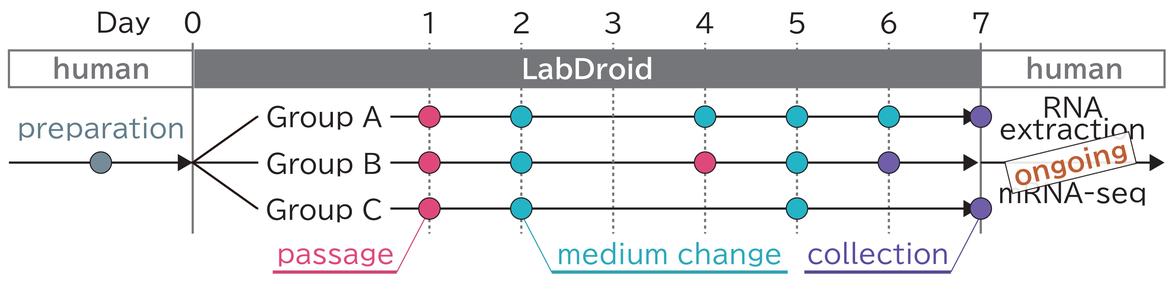




LabDroid completed 16 lines simultaneous, 456 hours continuous culture

- operation log makes robotic operation traceable
  →quantitative analysis:
  - operation / operation
  - operation / cell condition (see below card ↓)

iPS cell culture with different culture schedule



images of all Groups at collection time



LabDroid also performed complicated iPS cell culture without any errors

- different cell conditions can be linked culture operations quantitatively
- No worries about working on holidays and human-errors

★ I can’t culture iPS cells by myself, but I can try experiments using it now!

Quantitative operation x Quantitative analysis

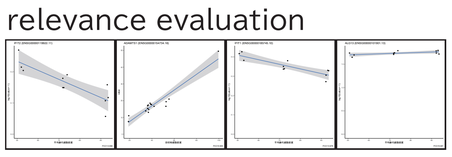
e.g. mRNA-seq

traceable operation

		#10 to Lifter Rack #3	
2	Prep. old plate	Plate transfer: 6-well plate (cell), Lifter Stocker #9 to Lifter Rack #2	
3	Prep. Trypsin	Tube transfer: 50-mL tube (Trypsin), Lifter Stocker #1#3 to Lifter Rack #1#3	
4	Prep. DMEM	Tube transfer: 50-mL tube (DMEM), Aluminium Bath #1 to Lifter Rack #1#1	
5	Prep. PBS	Tube transfer: 50-mL tube (PBS), Aluminium Bath #2 to Lifter Rack #1#2	
6	Add DMEM	Liquid transfer: Lifter Rack #1#1 (DMEM) to Lifter Rack #3 (new plate)	Volume 2400/2570/2670 µL; speed, 5
7	Discard DMEM	Aspiration: Plate on Lifter Rack #2 (old plate)	Plate tilt, 20 degrees; duration, 5 sec
8	Add PBS	Liquid transfer: Lifter Rack #1#2 (PBS) to Lifter Rack #2 (old plate)	Volume 2000 µL; speed, 1
9	Discard PBS	Aspiration: Plate on Lifter Rack #2 (old plate)	Plate tilt, 20 degrees; duration, 5 sec
		Liquid transfer: Lifter Rack #1#3 (Trypsin) to	

×

relevance evaluation



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principal component analysis

PC1	PCC
cell lysate handling time (37℃)	0.95
cell density at collection	0.70
RNA conc.	0.59
RIN	0.49
total culture time	0.42
cell density at passage_1	0.41

PC2	PCC
cell density at passage_1	0.49
cell density at passage_4	0.48
cell density at passage_5	0.45
cell density at passage_3	0.45
Avg. cell density at passage	0.44
cell density at passage_2	0.34

The relationship between operation and gene expression may become clear

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- monthly : Laboratory Automation monthly workshop
- yearly : LADEC（Laboratory Automation Developers Conference）



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