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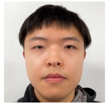
A dynamic scheduling method for autonomous maintenance of human iPS cells without human intervention.

Yuya Arai[a,b] ・ Haruka Ozaki[b,c]

a. Ph.D. Program in Humanics, School of Integrative and Global Majors, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki, 305-8575, Japan
b. Bioinformatics Laboratory, Institute of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki, 305-8575, Japan
c. Center for Artificial Intelligence Research, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki, 305-8577, Japan

Question & Comment



筑波大学 University of Tsukuba

1. Introduction

Background

- There is not flexible autonomous maintenance system for multiple human iPS cell lines.

Purpose

- We aim to make a scheduler for the autonomous maintenance and a simulator for its evaluation.

Keywords

- Multiple maintenance culture
- Single machine scheduling
- Dynamic scheduling

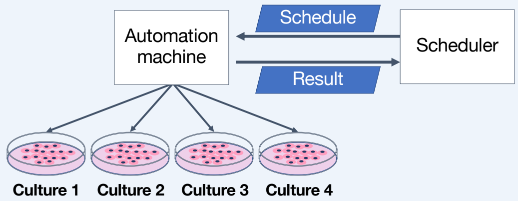


Figure 1 Visual abstract

2. Materials & Methods

Problem settings

- You want to continue maintaining human iPS cells.
- Maintainance are composed of several operations in a sequential manner.
- The next operation and its optimal time are determined according to the current operation and cell information (density and quality).
- The scheduler must determine when to perform each operation.
- Each type of operation has its priority.

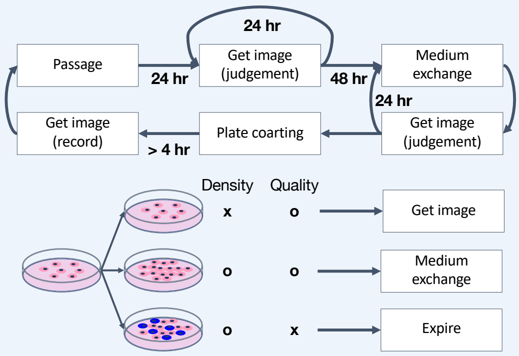


Figure 2 Culture state transition

Scheduler

- The objective function (S) is to minimise the total weighted earliness and tardiness for the optimal time ($\hat{t}$) of each operation.
  - $S = \sum_i W_i(|\hat{t}_i, t_i|)$
    - W_i: Weightd penalty function for i-th operation
- We use simulated-annealing algorithm for scheduling
  - To reduce variance due to stochasticity, scheduler runs parallel multi-threaded computations

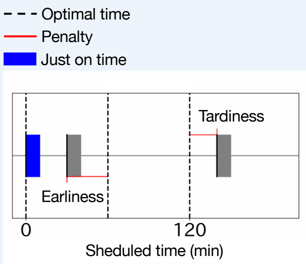


Figure 3 Objective function

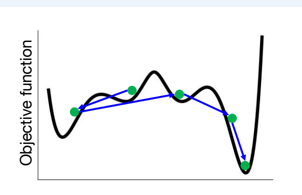


Figure 4 Simulated-annealing algorithm

Simulator

- The simulator simulates cell growth, changes in cell quality, execution of the entered schedule and returns results.
- The following conditions are assumed in this experiment.
  - Operation a failure probability $\mathrm{F}(a)$ is set constant ($\mathrm{F}(a) = 0$).
  - Each cell line has an independent growth curve.
  - Each cell line has a different initial state.
  - Cell quality of cell line i at timepoints t $\mathrm{Q}(i,t)$ is set constant ($\mathrm{Q}(i,t) = 1$).
  - The simulation ends when 500 operations have been performed.

3. Results

Simulation experiment

- The scheduler could continuously find schedules without error (overlapping schedule).
- The scheduler completed the simulation equivalent to 39.5 days in approximately 9 min.
- For each Cell line, eight to nine passaging operations were performed.
- The average time lag of execution of each operation was 4.28 min (blue dotted line in Fig.7).

Simulation result GIF

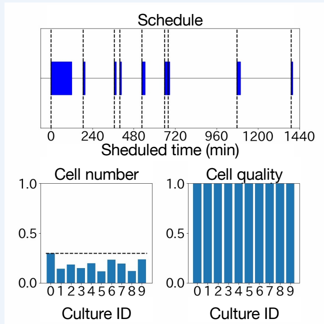


Figure 5 Simulation output

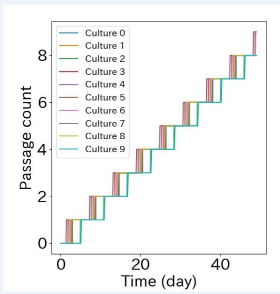


Figure 6
Total passage count

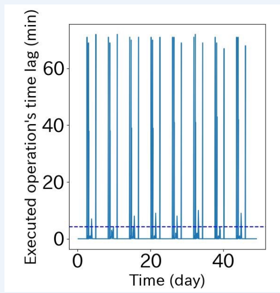


Figure 7
All executed operation's time lag

4. Discussion

Conclusions

- Establish the scheduler for autonomous maintenance of human iPS cells
- We conducted experiments with the simulator and confirmed that the scheduler works properly.

Future plan

- Simulation with real-world settings
  - Consumption of reagents
  - Operation failure (delay)
  - Observation error
- Real-world autonomous experiments

5. Acknowledgements

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