Design methodology of freeze-thaw processes   
towards industrial manufacturing of induced pluripotent stem cells  
iPS細胞の実生産に向けた凍結・解凍プロセスの設計手法

# Abstract

Towards industrialization of induced pluripotent stem (iPS) cells, there are many processes that require standardization. One example is the freeze-thaw process involving ultra-low temperature. The freeze-thaw process is required to transport and cryopreserve iPS cells. However, previous studies for iPS cells are still in infancy despite of its criticality; in fact, iPS cells are known to be vulnerable to freezing and thawing. In this study, I present models of heat and water transfer that can be used for designing the freeze-thaw process of iPS cells. In the simulation, it was assumed that iPS cells were placed with a cryoprotectant in a vial and cooled in a programed freezer or heated in a water bath. The first simulation was on heat transfer inside a vial during the freeze-thaw process. The second simulation was on mass transfer through the cell membrane during the freeze process. Significant difference was observed regarding freezing/thawing time and the cell volume after freezing depending on the combination, i.e., the diameter and the thermal conductivity of a vial are important design parameters.

# Equations

## Heat transfer

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## Mass transfer

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# Parameters

## Heat transfer

*T* Temperature [K]

*r* Radius [m]

Thermal diffusion coefficient [m2 s-1]

Thickness of ice [m]

Density [kg m-3]

Heat of fusion of ice [kJ kg-1]

*k* Thermal conductivity [W m-1 K-1]

Grashof Number [‒]

Acceleration of gravity [m s-2]

Kinematic viscosity coefficient [m2 s-1]

Prandtl number [‒]

Rayleigh number [‒]

Nusselt number [‒]

Height of the vial [m]

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l Water

s Ice

v Vial

sf Surface of the vial

e Air

## Mass transfer

Volume flux of water [m3 m-2 s-1]

Permeability coefficient [m s-1 Pa-1]

Osmotic pressure difference [Pa]

*C* Concentration of the solute [mol m-3]

*v* Molar volume [m3 mol-1]

*a* Activity [‒]

*V* Volume [m3]

*n* Amount of substance [mol]

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w Water

0 Reference

ex Extracellular

in Intracellular

sol Solute