**Out of Body Vitro Condition**

**2019 Faria**

How to know which one is better?

1. ~~Experiment~~
2. Math Model

Experiment:

Doing Research on Particles/Cells etc will face lots of difficulties (Can only done **Qualitatively** (only detect if it’s successful, rather statistically)), since:

Every experiment can vary by conditions:

* 1. Environment: concentrations, injection time, temperatures
  2. Nature of Cells: Type, Size, fluorescence strength, cell movements
  3. Design: Method of Injection, Detection, etc

Therefore, Dosimetry (Measurement) can vary a lot, with data uncertain

Thus, Need Math Equations to solve, For **Quantitative** analysis (increases how much etc)

Math Solving: Combine these two together for **Experiment Use in Vitro** (In solution, Lab Environment)

1. Association Model: Biological Interaction with Cells-Particles
2. Dosimetric Model: Particle Movements in Vitro (out of body, in solution, lab-related)

* : function of Dosimetry parts, {on cells: Logo

  Description automatically generated; not on cells: 0}
* ： Function of Association parts (cell related)

Table

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1. SC: surface coverage of cells (How many cells) Pos
2. r: rate of association (particle into cells rate) Pos
3. u: Concentration of Particles Pos
4. P\_capactiy: Cell’s **inside** capacity for particles Pos
5. P\_assoc: num of particles **inside** cells Neg
6. S\_capacity: Cell’s **Surface** capacity for particles Pos

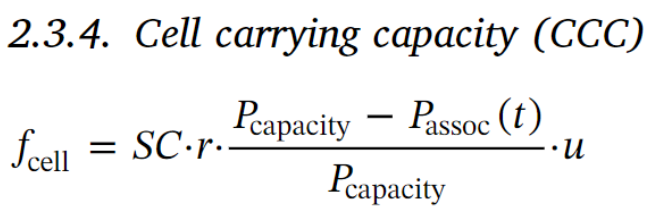
Visualise:

Incubate Cells(1,2) => Put Particles into fluid(3) => Particles move onto cells’ surfaces(6) => Particles move from surfaces into Cells(4, 5)

Performance Measure:

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Description automatically generated , (0<P<1), where err\_best is fixed and err\_model is current one

Best Model:  --------Indicates S\_capacity is not important (threshold may be P\_ instead, association speed rather than surface capacity)

Determine Association rate **r** :

Bigger, larger cell may have high **association(brighter, settling faster),** but may not have high **Association rate r** .(Easy to identify but may not be efficient)

Targeting Behavior is shown, but still phagocytic cell can still associate many particles

A further experiment given different conditions leads to same association rate r, (meaning r is more cell-oriented and independent of experiment elements)

Conclusion:

* Found rate of association r, this parameter stands for characteristics of cells (independent of environment). Enable us to do quantitative analysis by using it (control variables of environmental elements)
* Math Modelling: model association rate considering environmental elements as well

Questions:

Why does this report mention **phagocytic** a lot?

**Diffusion Formula:**

Text

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**Sedimentation Velocity:**

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**Surface Area:**

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**LIVER Absorption**

**Factors affecting number of Particles entering Hepatocyte**

Particles enter human body(blood vein) -> [impede by Kupffer Cells] or [through vein window] –> into space between hepatocytes and vein -> enter hepatocytes -> exit hepatocytes -> Enter Bile Duct

Factors need to consider:

1. Particles (use **Concentration Function** that we have already solved?):
   1. Size
   2. Type
   3. Concentration
2. Vein
   1. Blood Speed (Heart Rate)
   2. Fenestrae size (windows on central vein): impact more on larger particles. Source: <https://www.nature.com/articles/gt200860#:~:text=In%20the%20current%20study%2C%20we,is%20107%C2%B11.5%20nm>.
   3. Kupffer Cells: Roadblocks, (impact more on **larger** particles), Negative Correlation

F\_kupffer = Remaining Capacity/Particle\_Size

**F\_vein = C\_fenestrae \* F\_kupffer**

1. Space In Between:

**F\_****space = F\_fluid = -D\*delta\_u + s\*u**

1. Hepatocytes (can we just use **F\_cell** directly? With discharge rate added):
   1. Absorption rate: Positive Correlation
   2. Discharge rate: Positive Correlation
   3. Capacity: Positive Correlation
   4. Quantity: Positive Correlation

**F\_hepatocytes = F\_cell of CCC model**

1. Bile Duct:
   1. Concentration
   2. Circulation speed

**F\_bileduct = Speed \* (1/Concentration)**

**In total:**

u = concentration of particles inside Hepatocytes

d(u)/d(t) = F\_kupffer \* C\_fenestrae \* F\_vein \* F\_space \* F\_hepatocytes \* F\_bileduct

**In Body Vivo Condition**

**2019 ACS**

**Assume** Non-Biodegradable NanoParticles? As they can degrade and get easily excreted from the body.

Nanoparticles can be used as medical or treatment method of human body.

After injection of particles into human body, two ways to get them out:

1. Through Kidney(renally) and urinary (Size<5.5nm can go through kidney filtering): Well Studied
2. **Through Liver and Feces, Hepatocyte cell: Not so learnt yet**
3. Self Biodegradable, at its own

large, nonbiodegradable, inorganic nanoparticles

Main Reasons:

liver nonparenchymal cells (e.g., Kupffer cells and liver sinusoidal endothelial cells)

**Kuppfer Cells:**

Sequester nanoparticles, also implies other liver nonparenchymal cells interact as well

**endothelial cells:**

act as a lowpass filter that excluded or impeded the extravasation of Particles

larger than their fenestrae size (Gap between each endothelial cell)

* Transcytosis, Instead of going through