Nanoparticle Toxicity
An Introduction

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Outline

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3. Experiments
4. Experimental Results
5. Some Modelling Assumptions
6. Modelling Uptake

Next talk:

1. Compartment Model
2. Parameter Estimation
3. Modelling Results
4. Future Work

Introduction

- Nanoparticle: 1-100nm (human hair $\sim$ 50,000 nm).
- Quantum dots: nanoparticles made from semiconductor materials - CdTe here.
- *Size-tunable optical properties:* green-emitting 2nm, red-emitting 5nm QDs (less aggressive).
- Applications: high-resolution cellular imaging, drug delivery, tumour targeting.

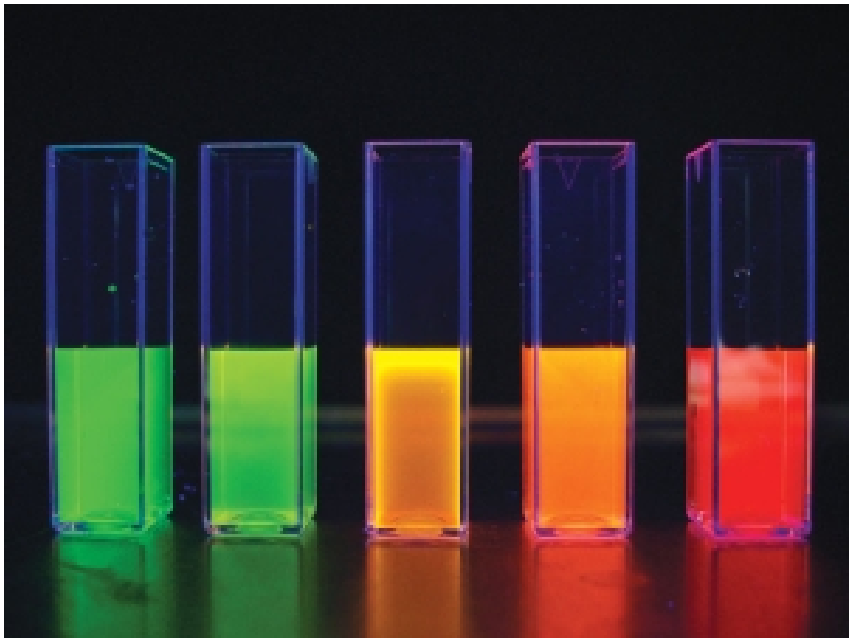


Figure: Various sizes of QDs

Gun'ko group, TCD

Biology

- Cell exposure to QDs:
  - Cytoplasm granulation
  - Loss of functionality
  - Nucleus fragmentation
  - Chromosome damage
  - Cell death
- Need to minimize damage:
  - QD composition
  - Dose
  - Exposure time

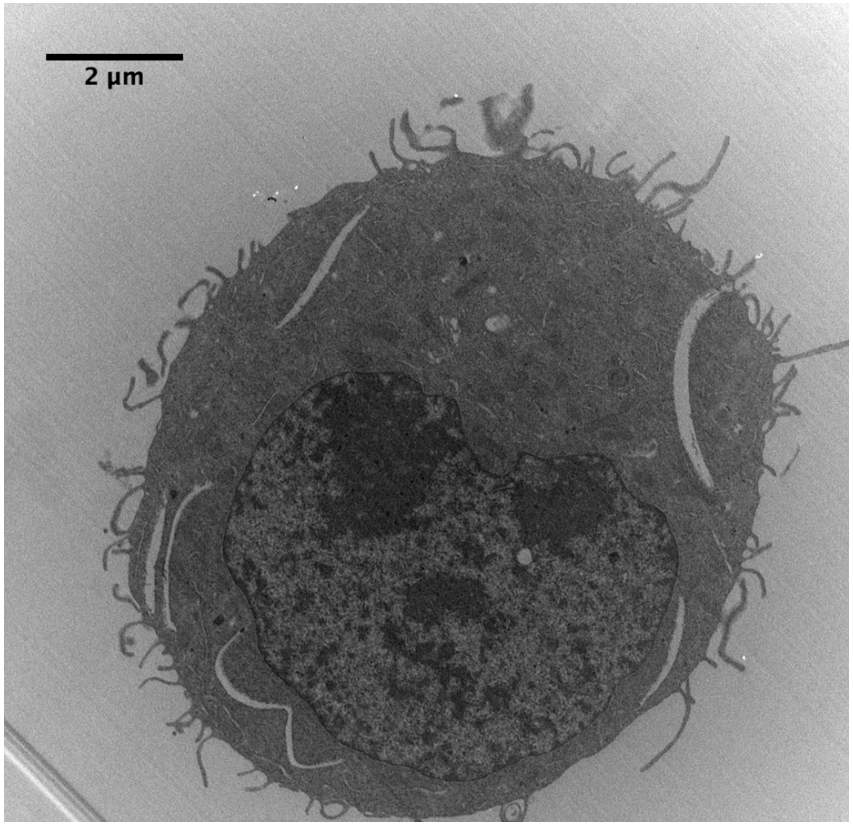


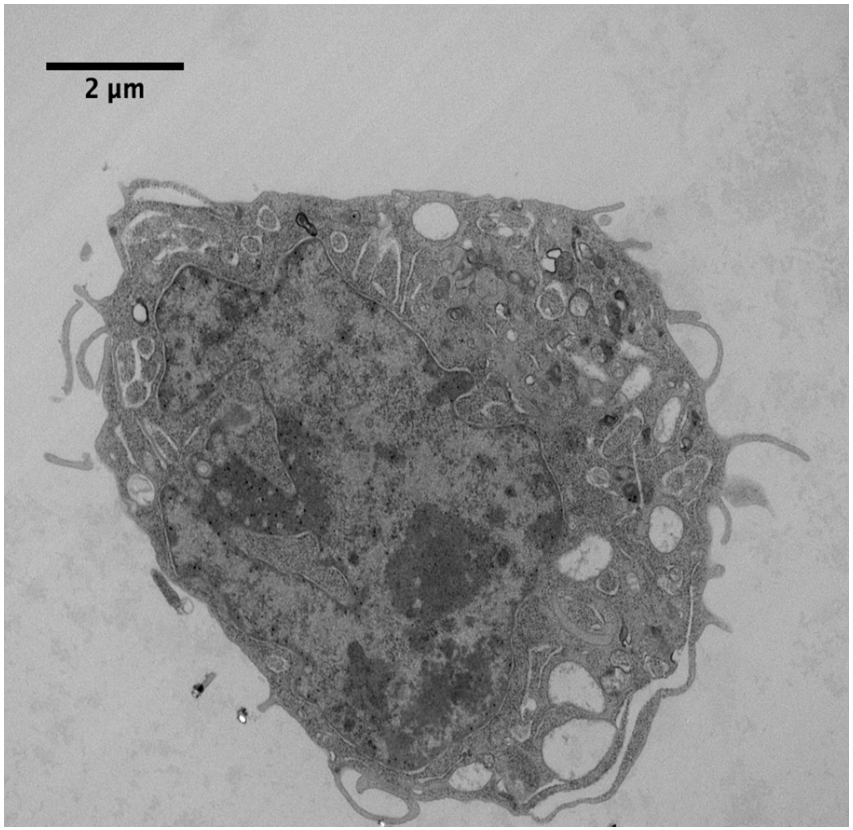
Figure: TEM image of untreated RAW 264.7 cell (control)

Experiments

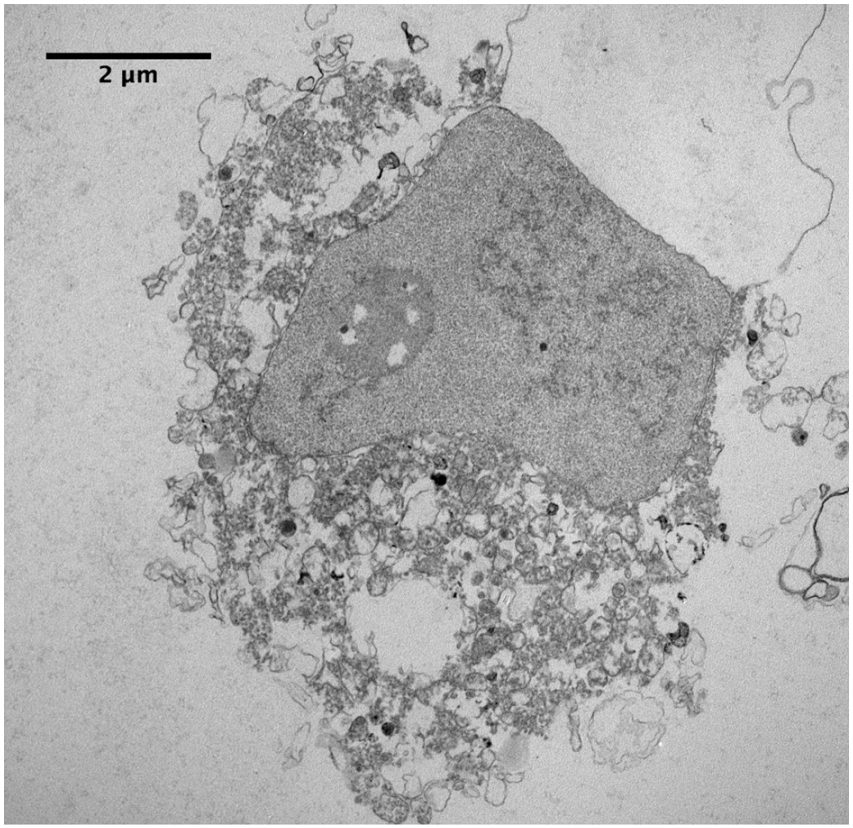
- Cells grown for 24 hours.
- Co-incubated with coated or uncoated green/red QDs for 12/24 hours.
- Three concentrations: 1 nM, 10 nM, 100 nM.
- Analyzed using a flow cytometer (identify if cells are healthy, in apoptosis, or in necrosis).

Results

- 1 nM, 10 nM: no deviation from control.
- Drastic change for 100 nM.
- Varied greatly depending on QD parameters.



Cell with Green TGA QDs



Cell with Red TGA QDs

Some Modelling Assumptions

- Four states: healthy, apoptotic, necrotic, dead.
- Healthy cells can enter apoptosis or necrosis.
- Cells in apoptosis or necrosis can die.
- No reversibility.
- Rate at which cells leave healthy state depends on QD concentration.

Modelling Uptake

- Cells uptake QDs via endocytosis.
- Depends on cell type, NP size, shape, surface treatment.
- No data on uptake rates!
- Define a saturation concentration c_s and current intracellular concentration $c(t)$.
- Assume rate of ingestion of proportional to difference between c_s and $c(t)$ so

$$\frac{dc(t)}{dt} = k_c(c_s - c(t)),$$

with $c(t = 0) = 0$, giving

$$c(t) = c_s(1 - e^{-k_c t}). \tag{1}$$

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References


Olga Gladkovskaya, Paul Greaney, Yurii K. Gun'ko, Gerard M. O'Connor, Martin Meere and Yury Rochev.
An experimental and theoretical assessment of quantum dot cytotoxicity.
Toxicology Research, 2015, **4**, 1409–1415