Heterogeneous multiscale simulations of radiation therapy with gold nanoparticles

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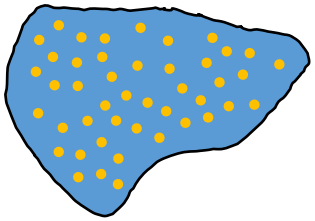
Carleton UNIVERSITY

Gold **N**ano**P**article dose-enhanced radiation **T**herapy (**GNPT**)



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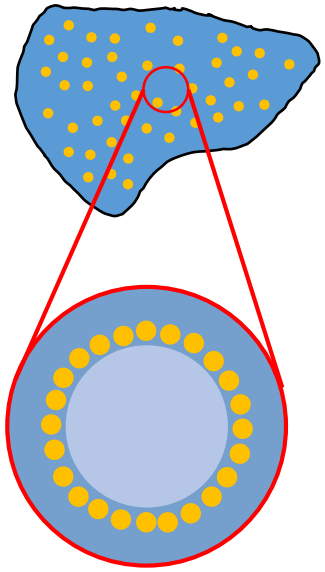

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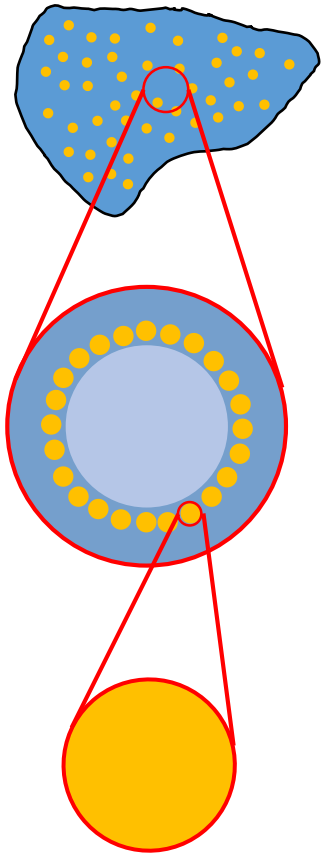

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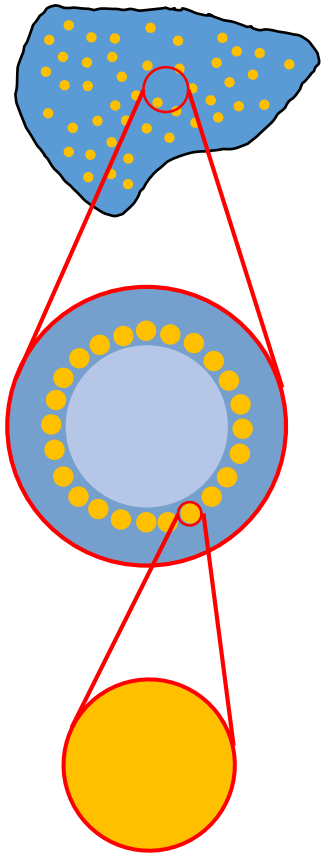

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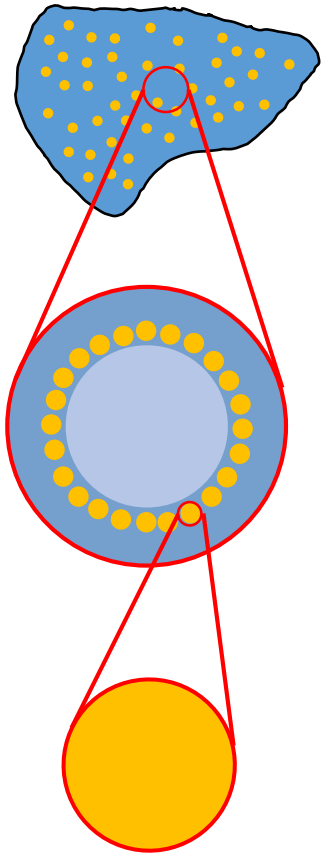

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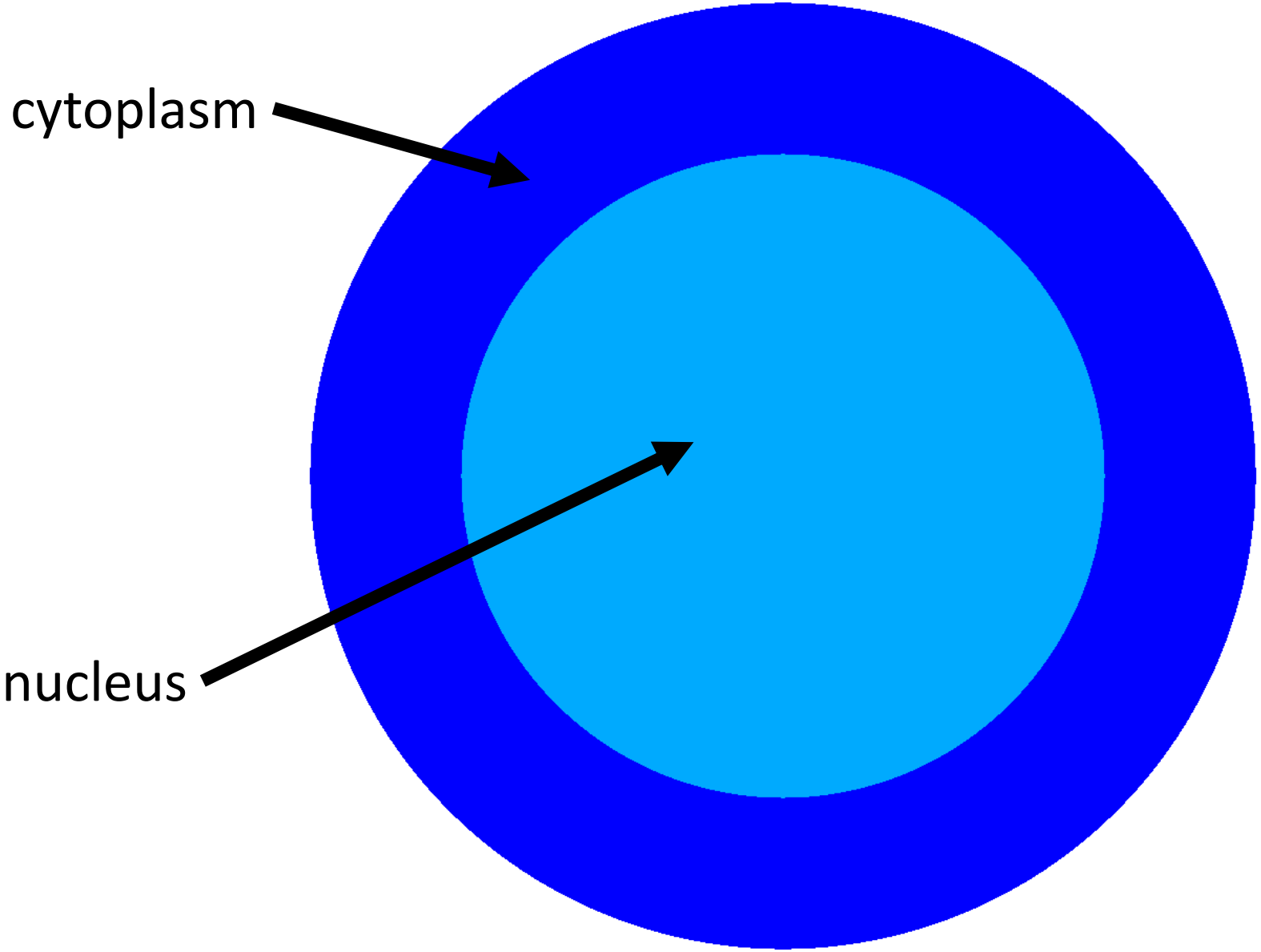
Overview

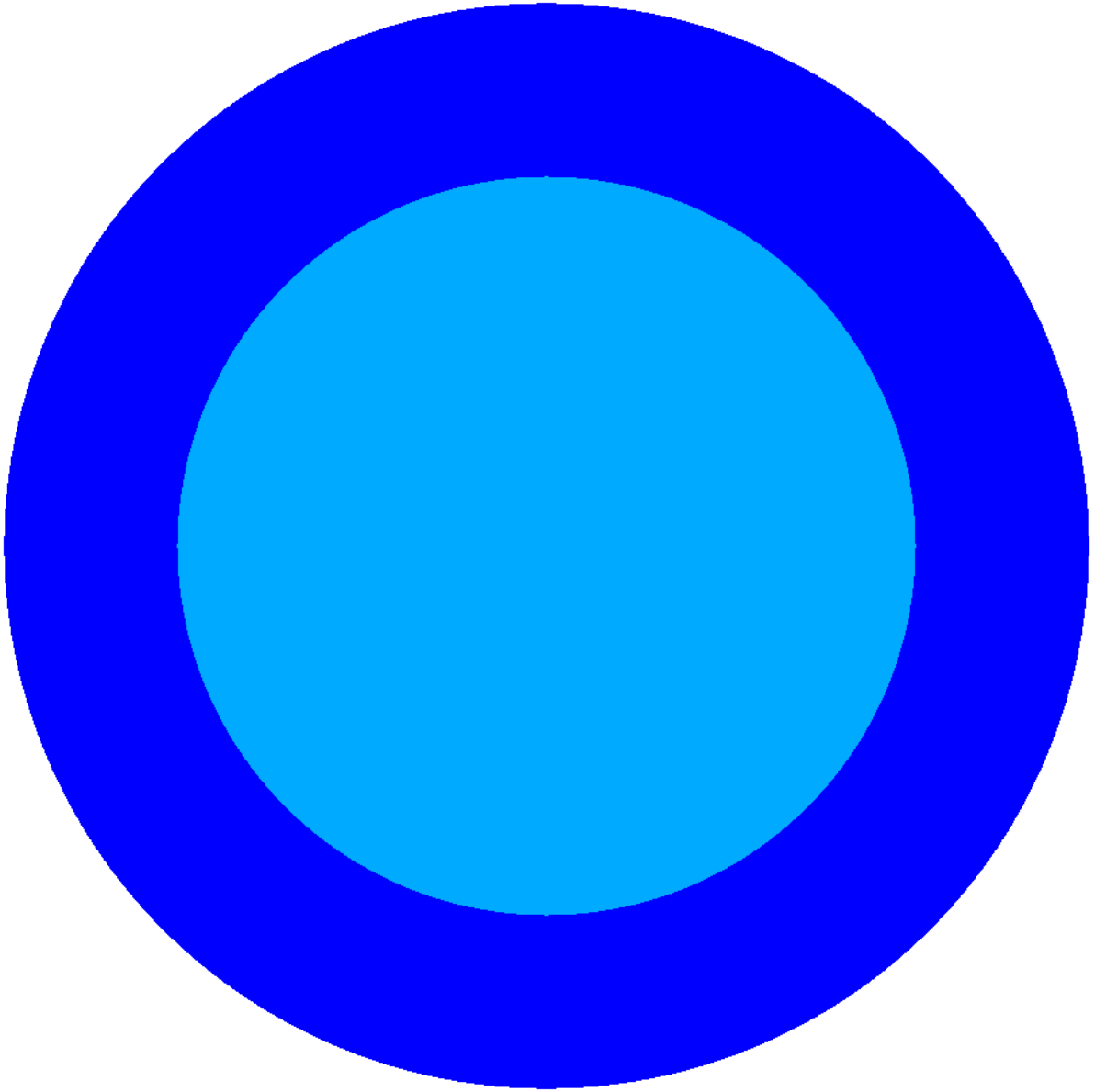
- Modelling cell and GNP geometry
- Heterogeneous Multiscale Model
  - Introduction
  - Creating a scoring volume
  - Full phantom model
- Results

Cell Model - no gold



Cell Model – modelling the gold shell

- GNPs collect on the surface of the nucleus



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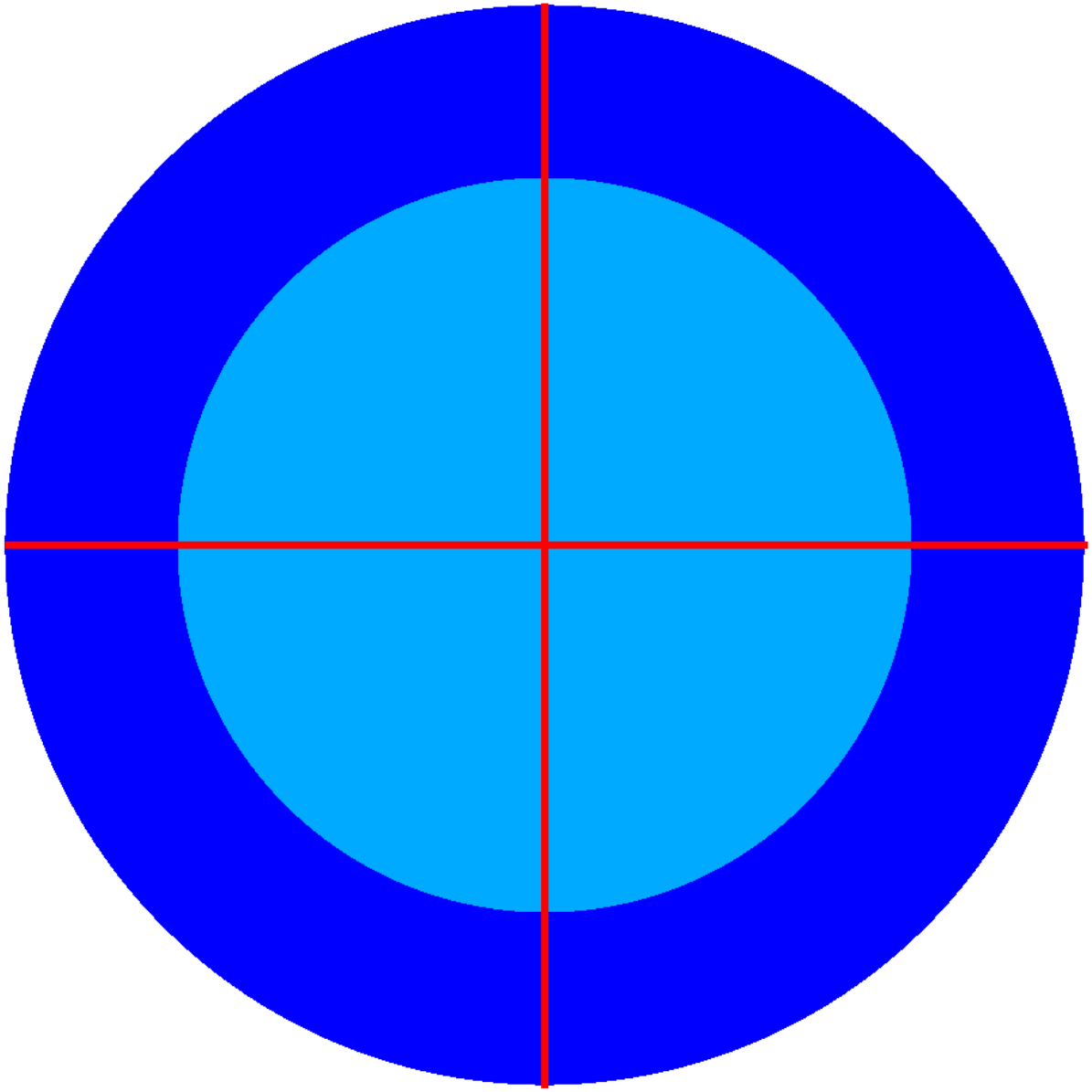

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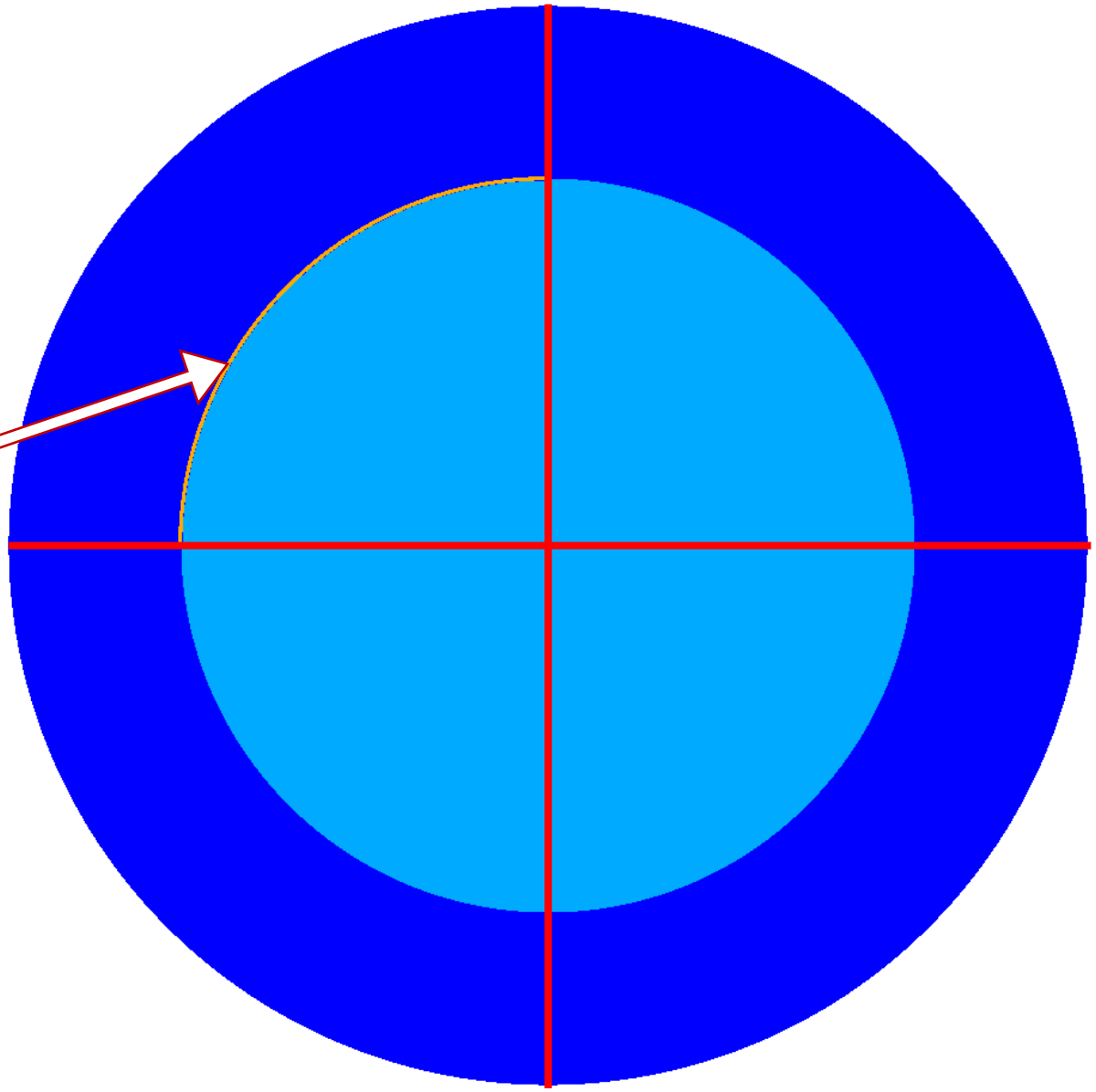

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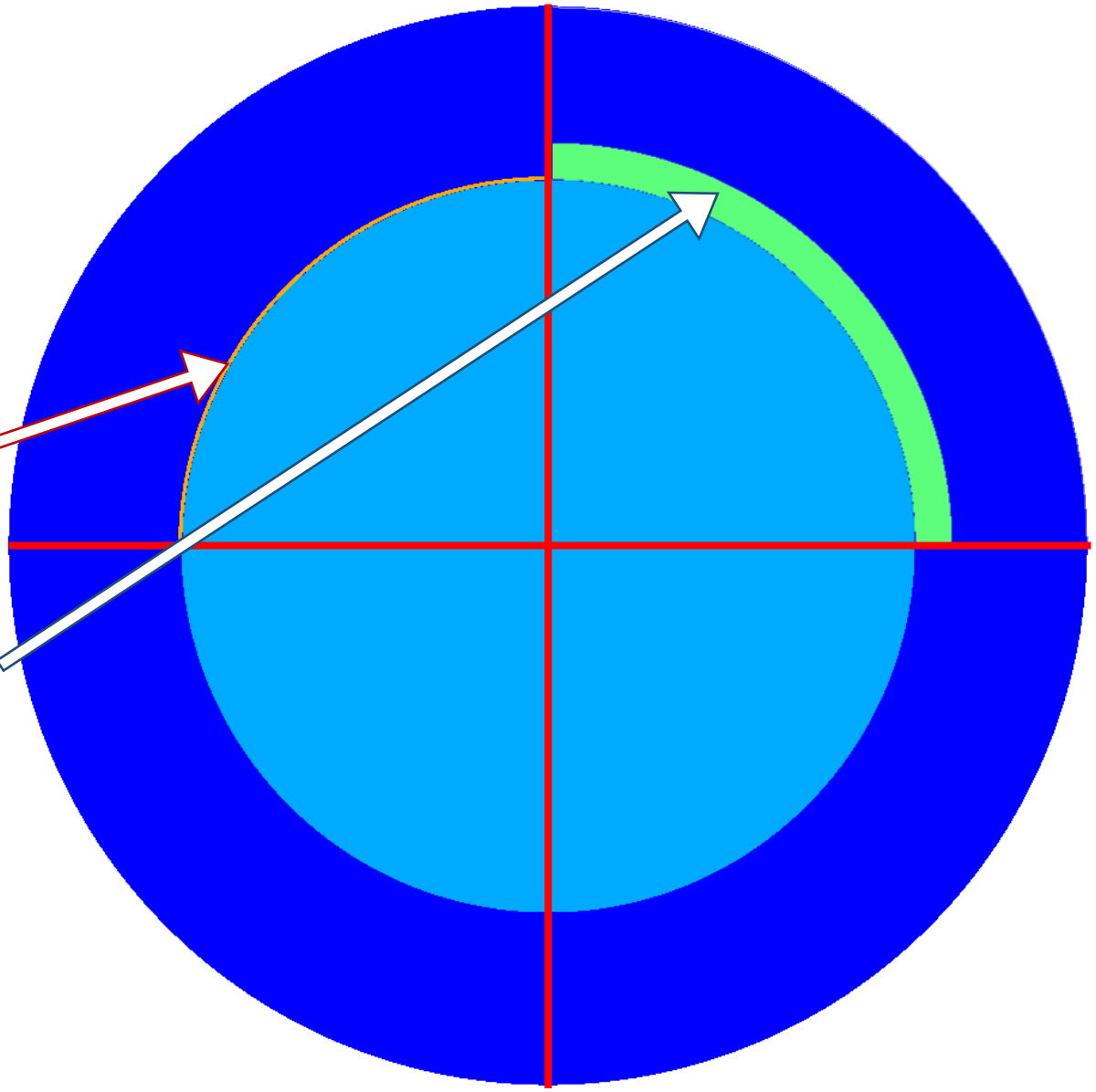

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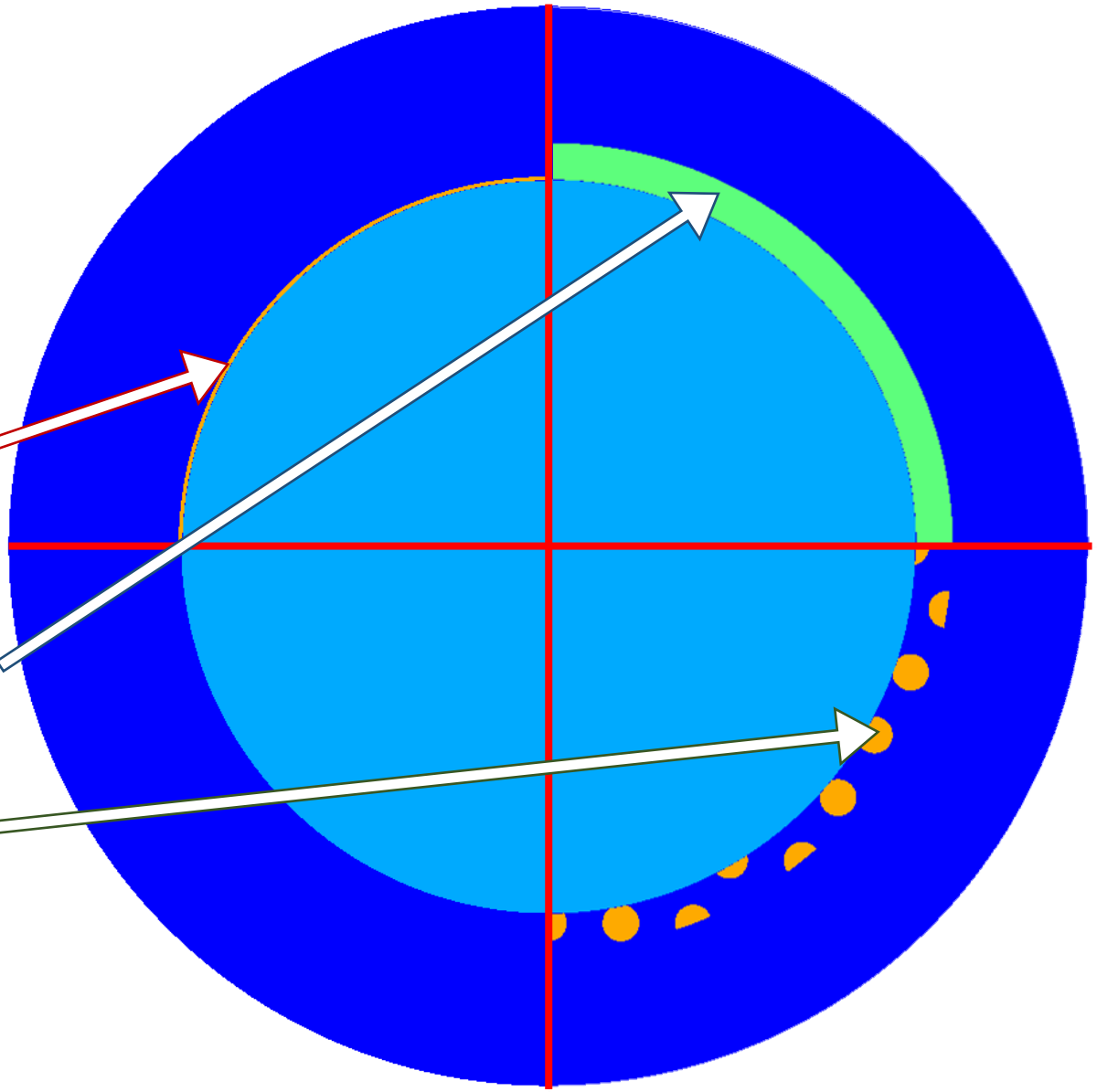

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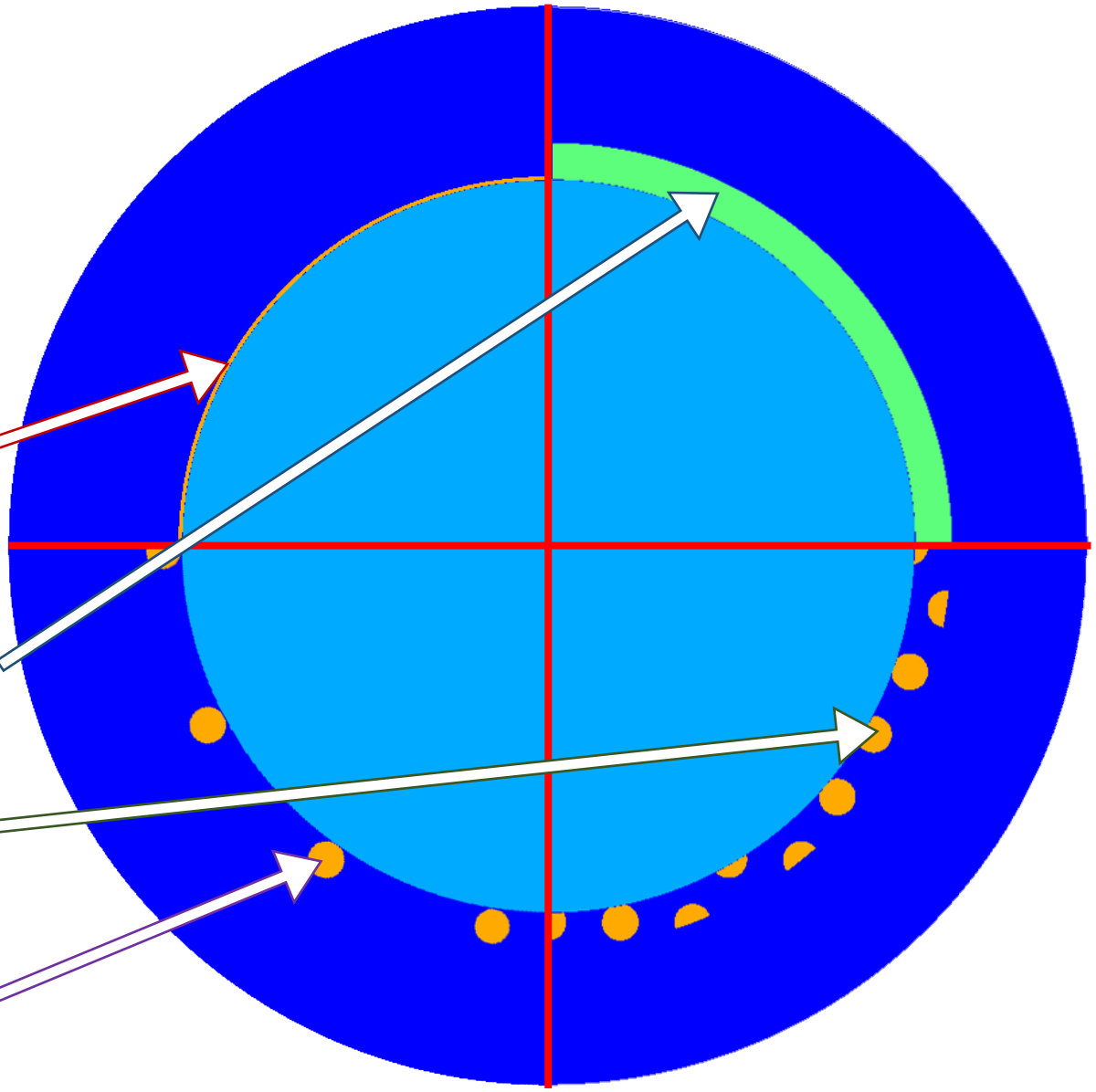

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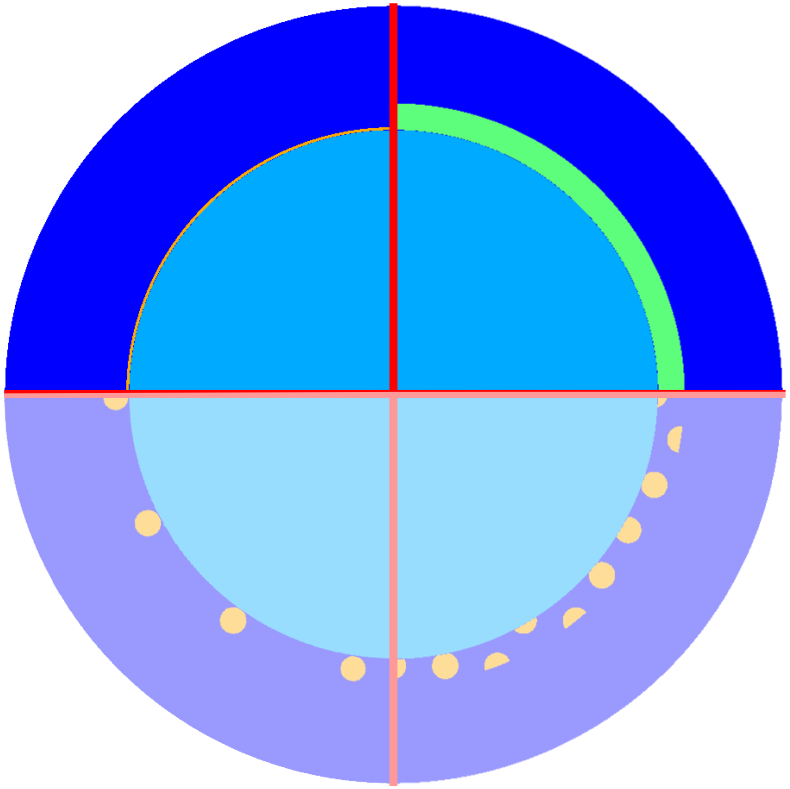

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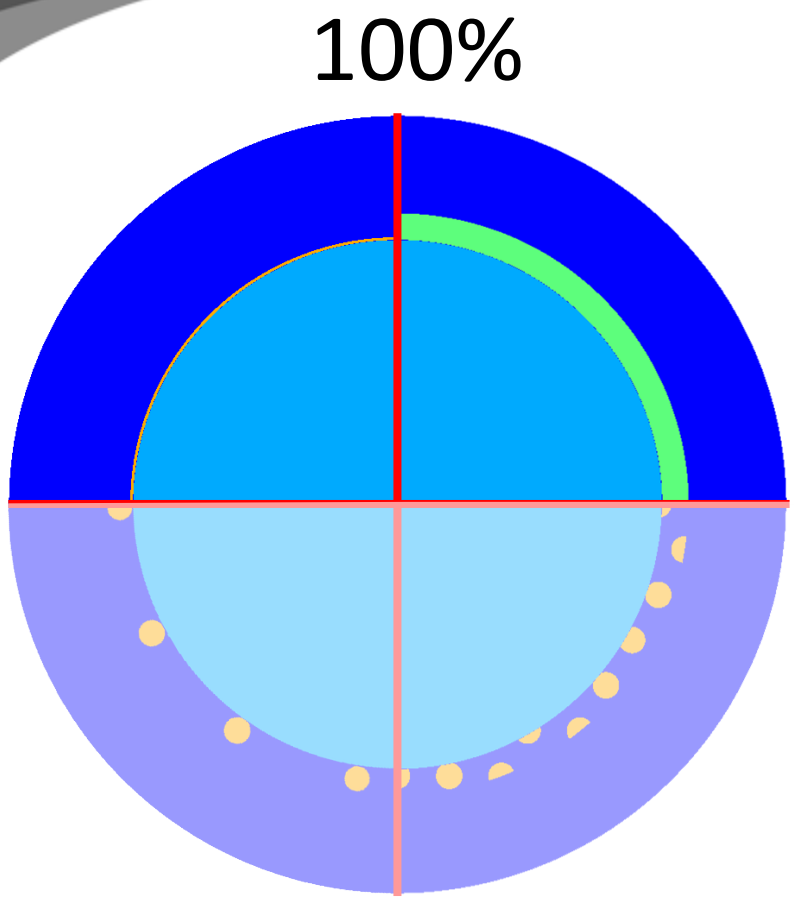

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Single CPU simulating 1E8 histories with 25 nm diameter GNPs on an Intel(R) Xeon(R) CPU E5-2667 v4 @ 3.20GHz

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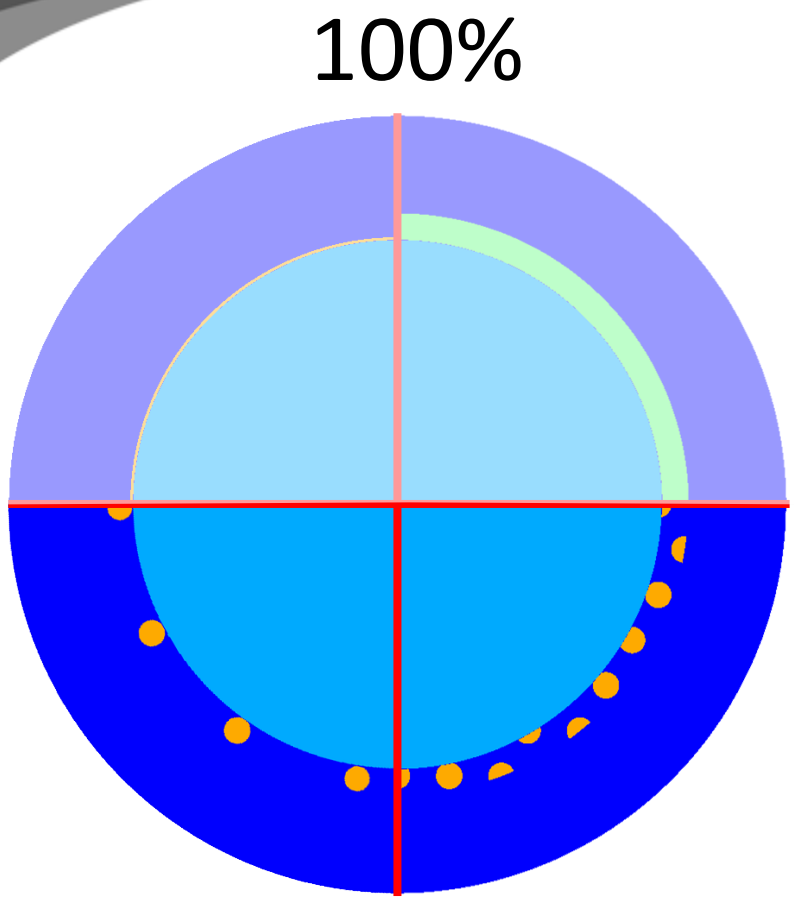

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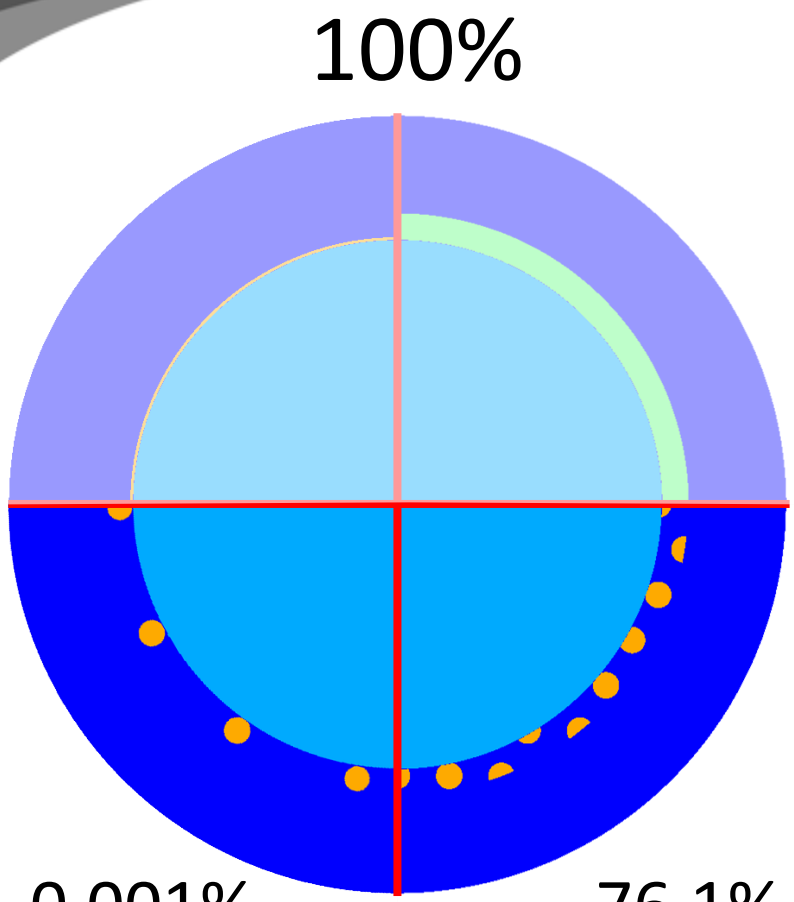

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- Lattice geometry is up to ≈69,000 times faster than spiral configuration

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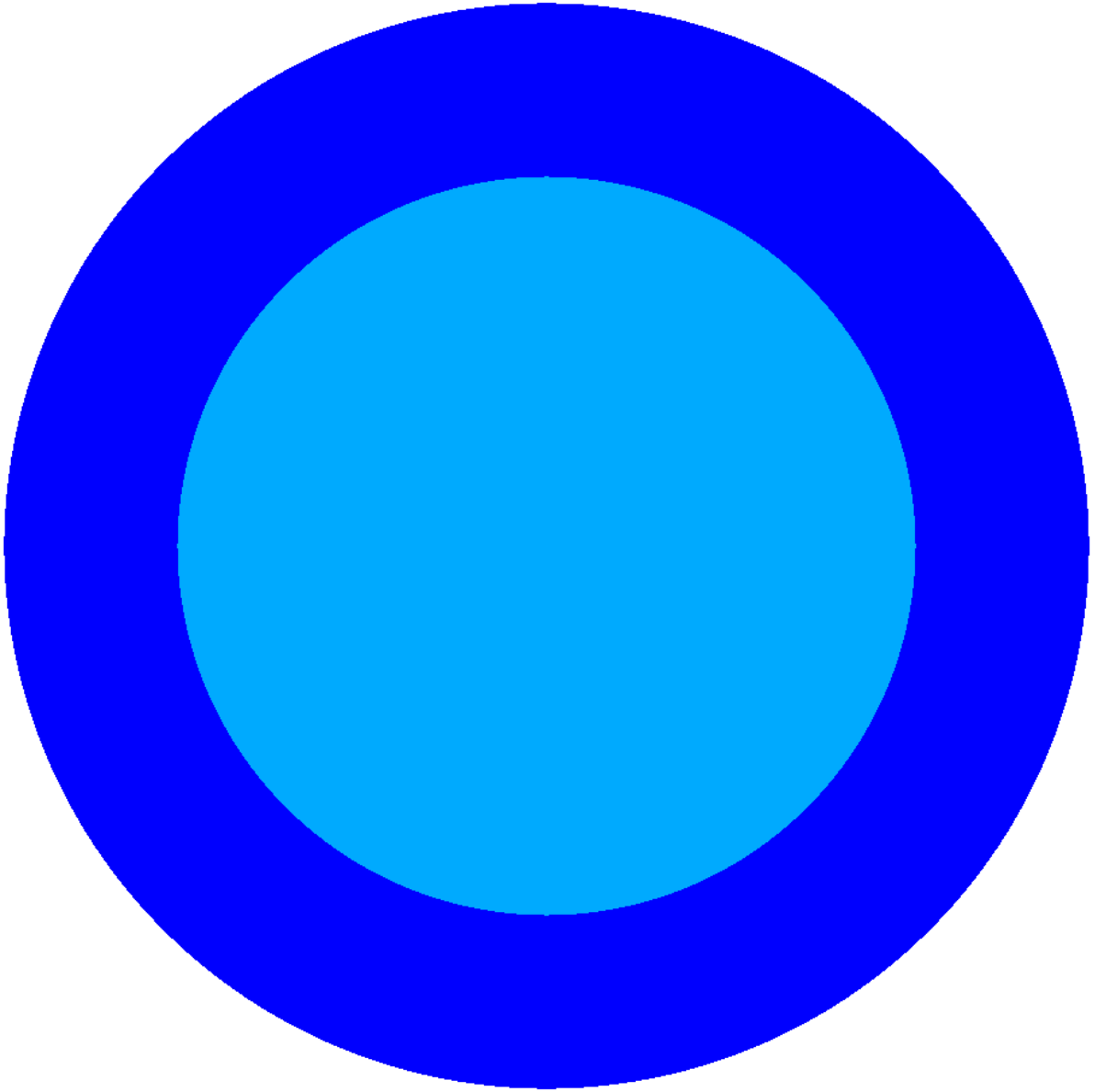
Cell Model – modelling gold filled endosomes

- GNPs collected in a tightly packed compartment



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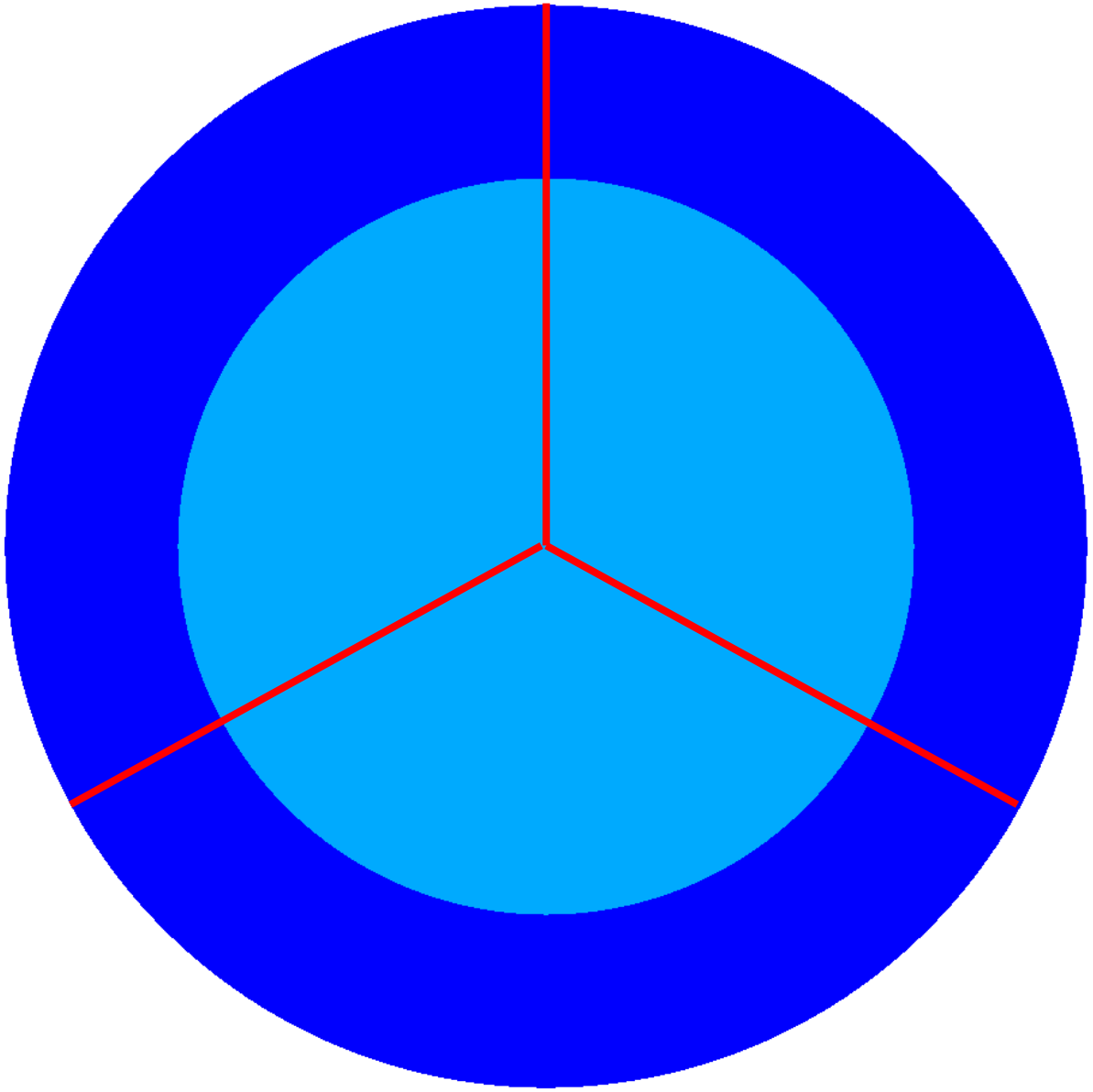

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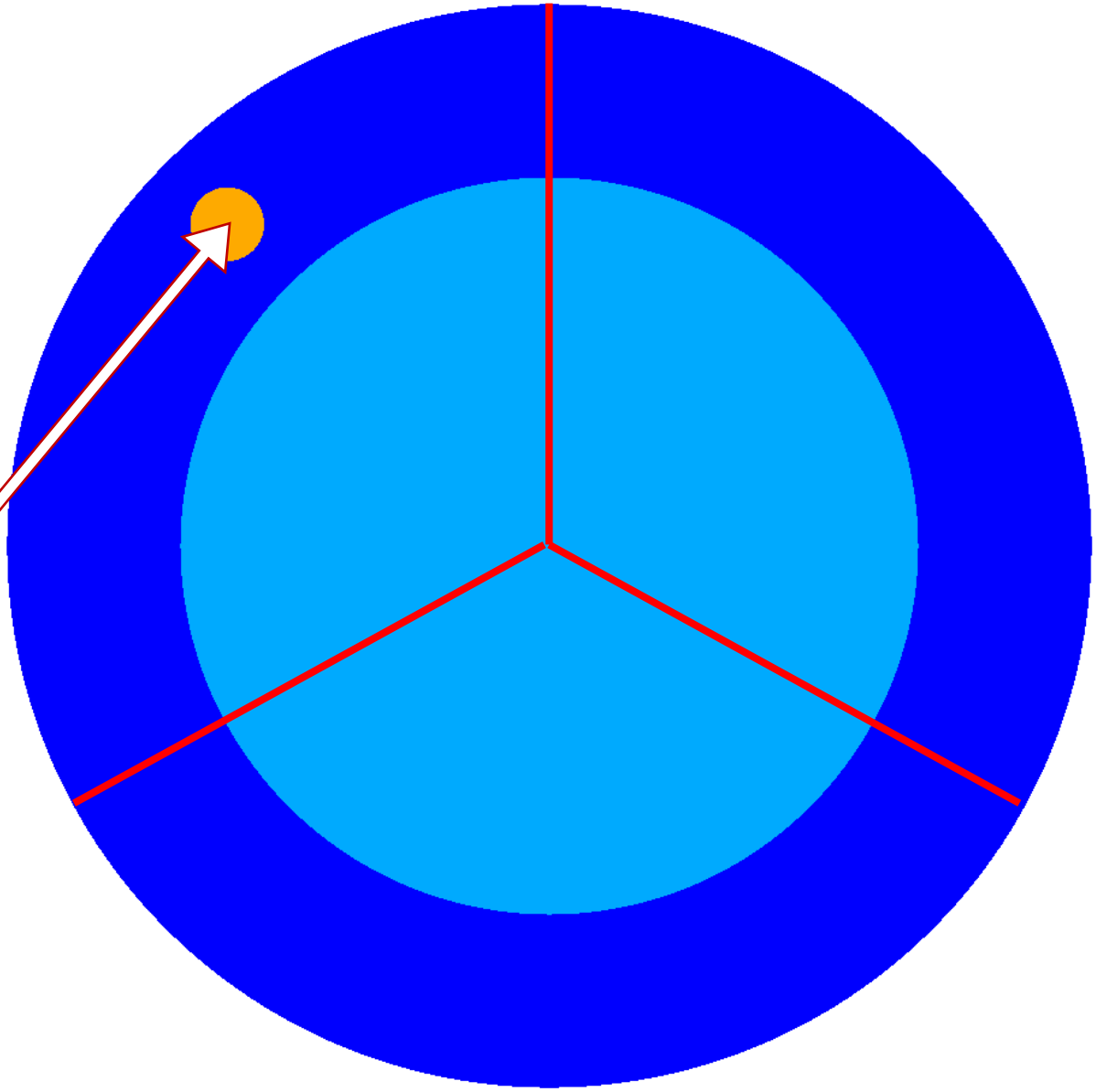

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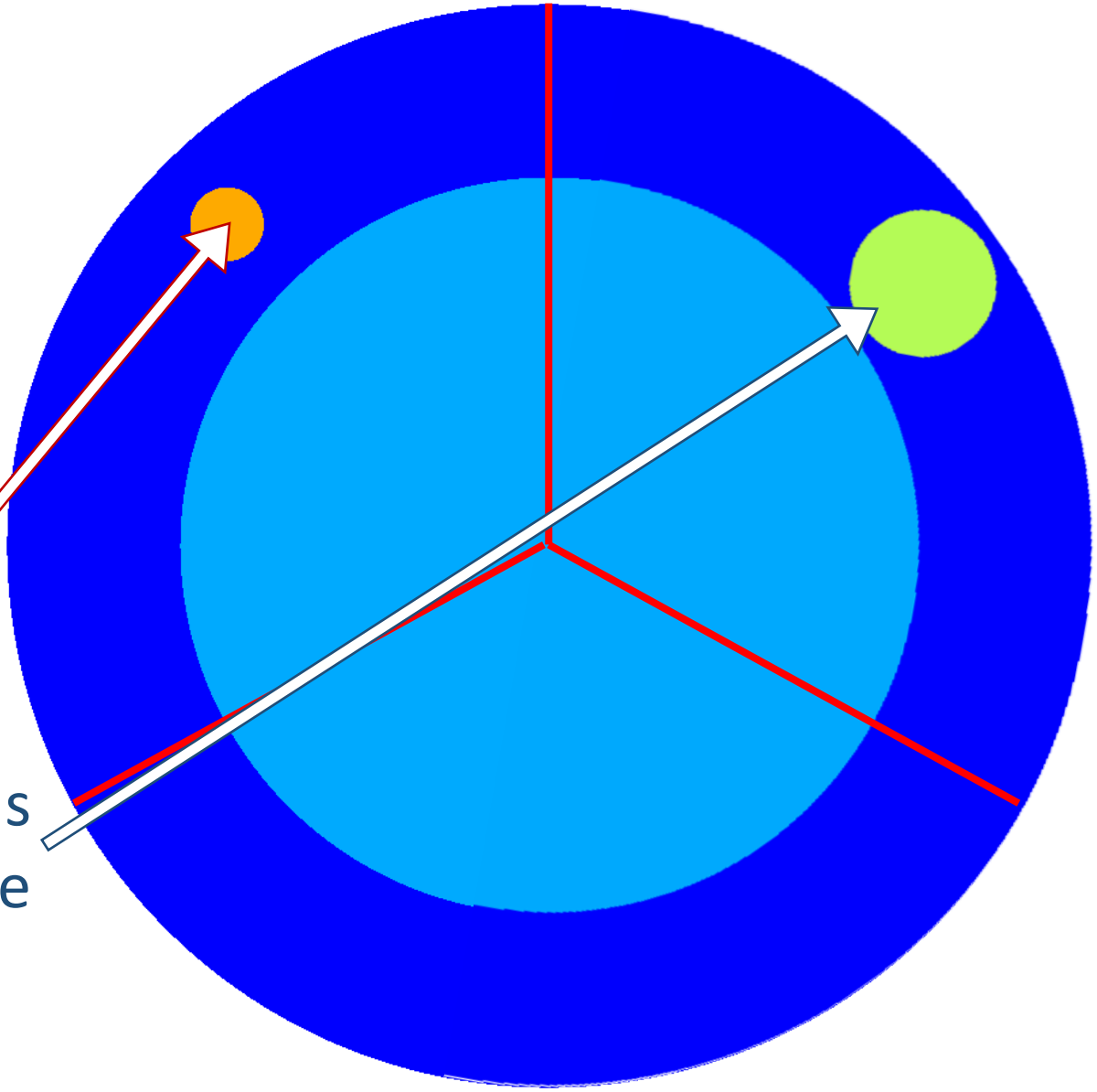

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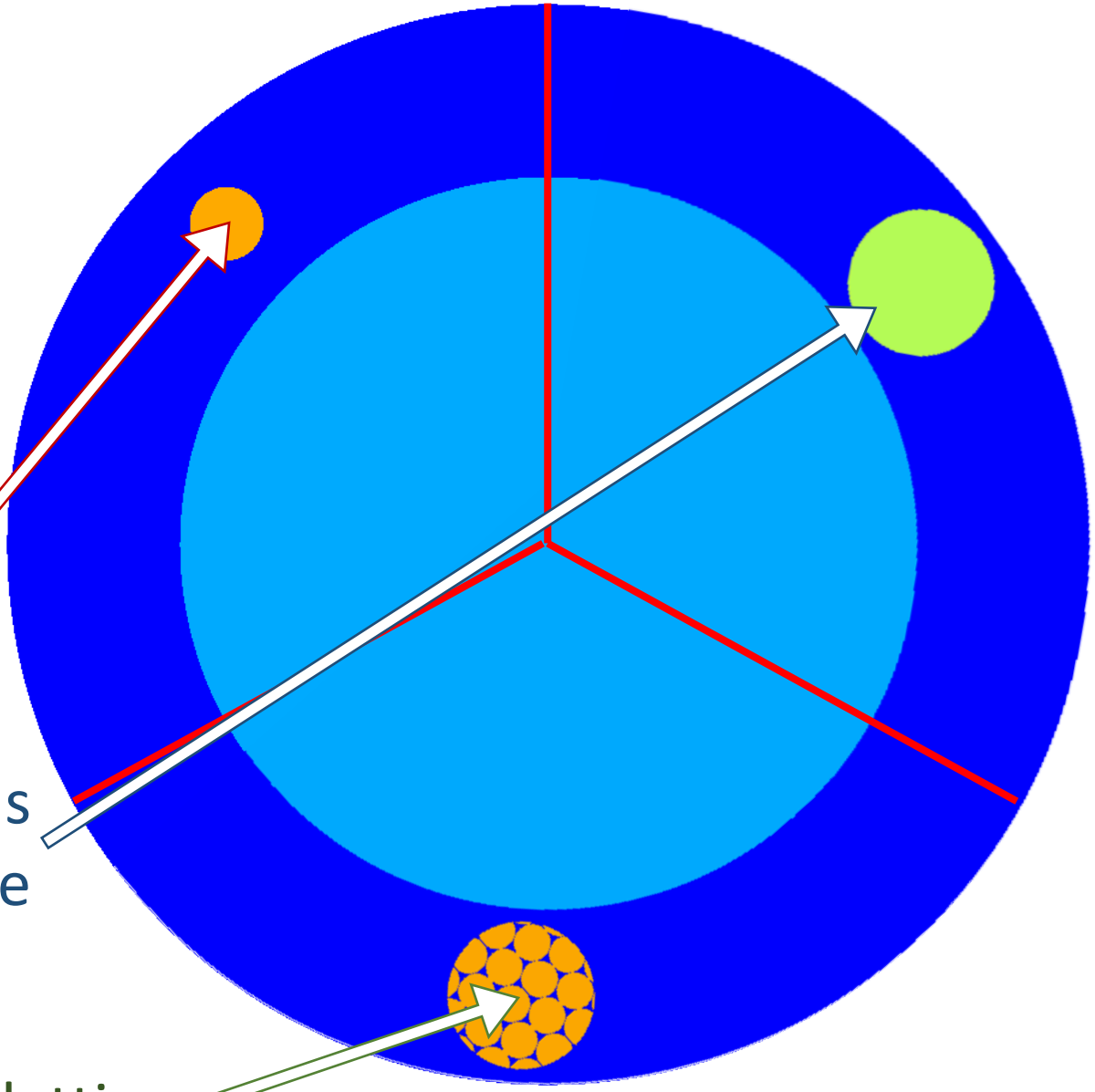

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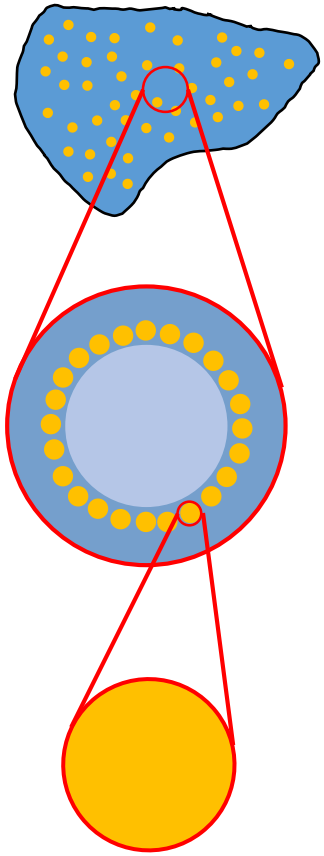

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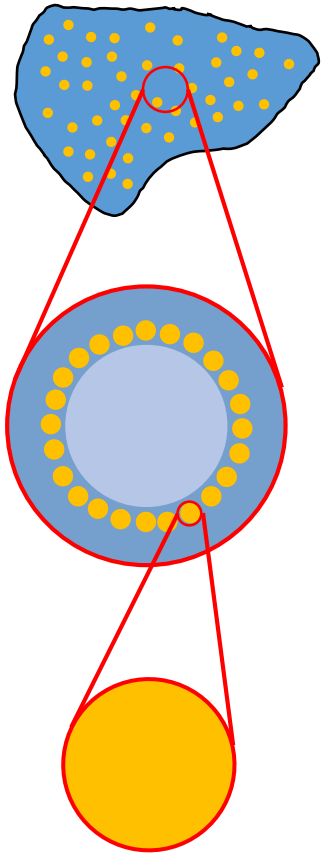

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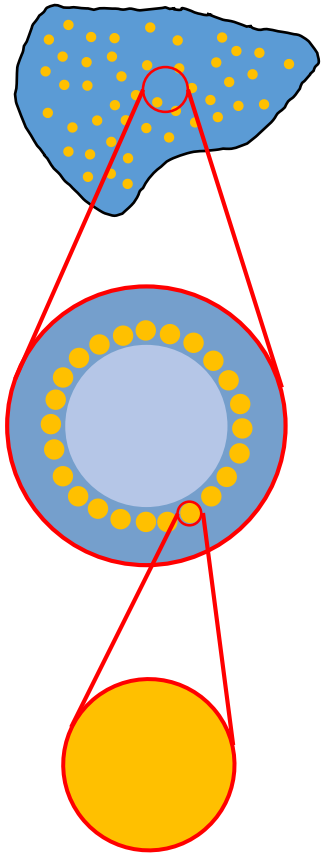

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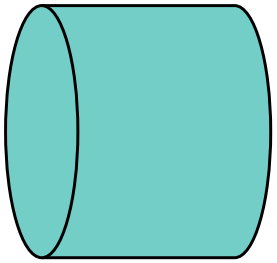

Single medium
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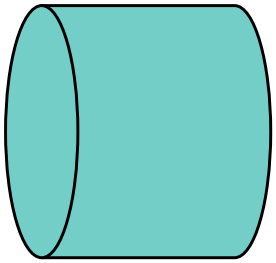

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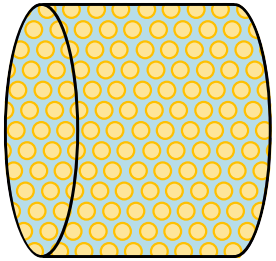

Microscopic structures
modelled separately

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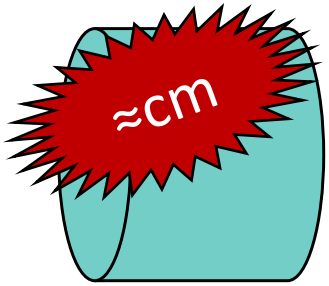

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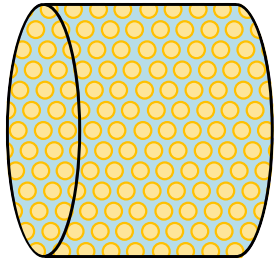

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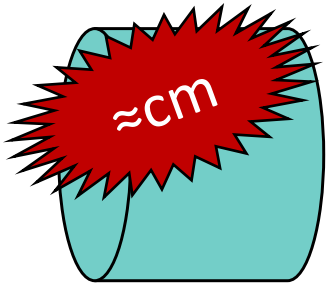

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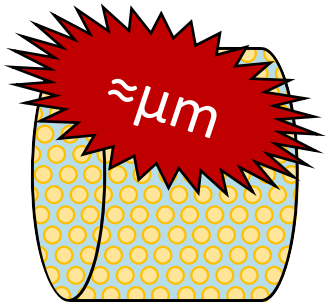

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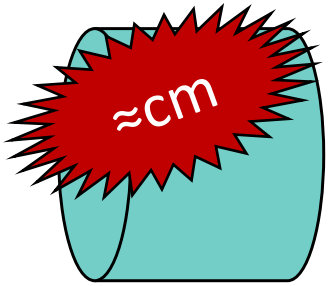

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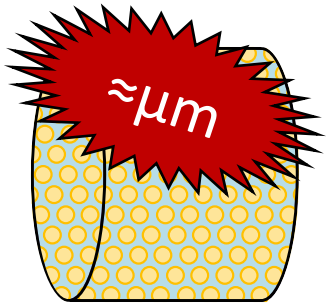

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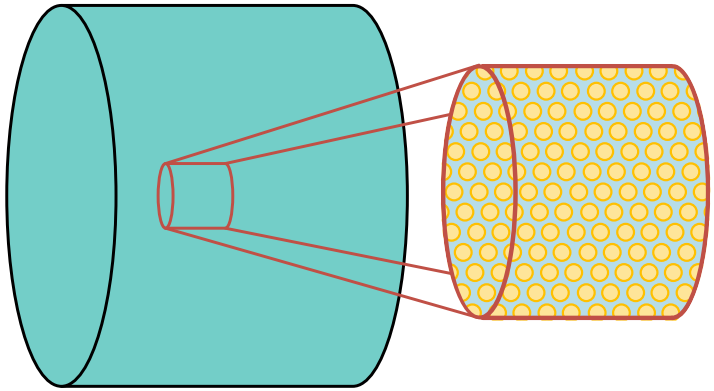

Heterogeneous
Multiscale model

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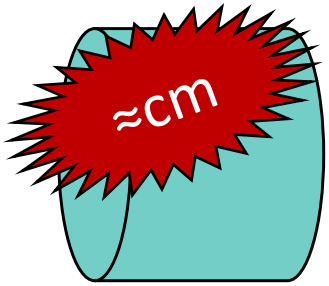

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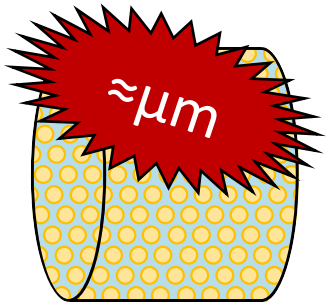

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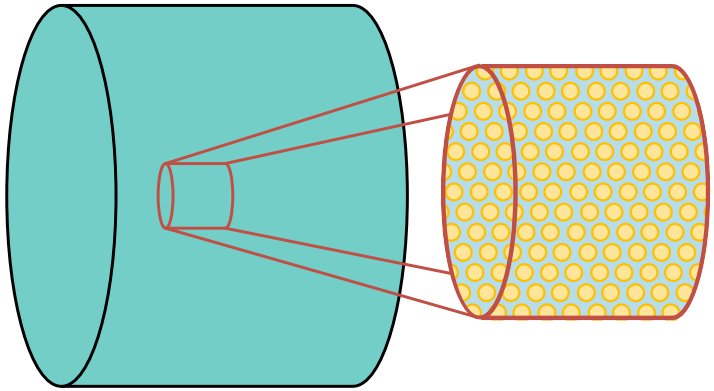
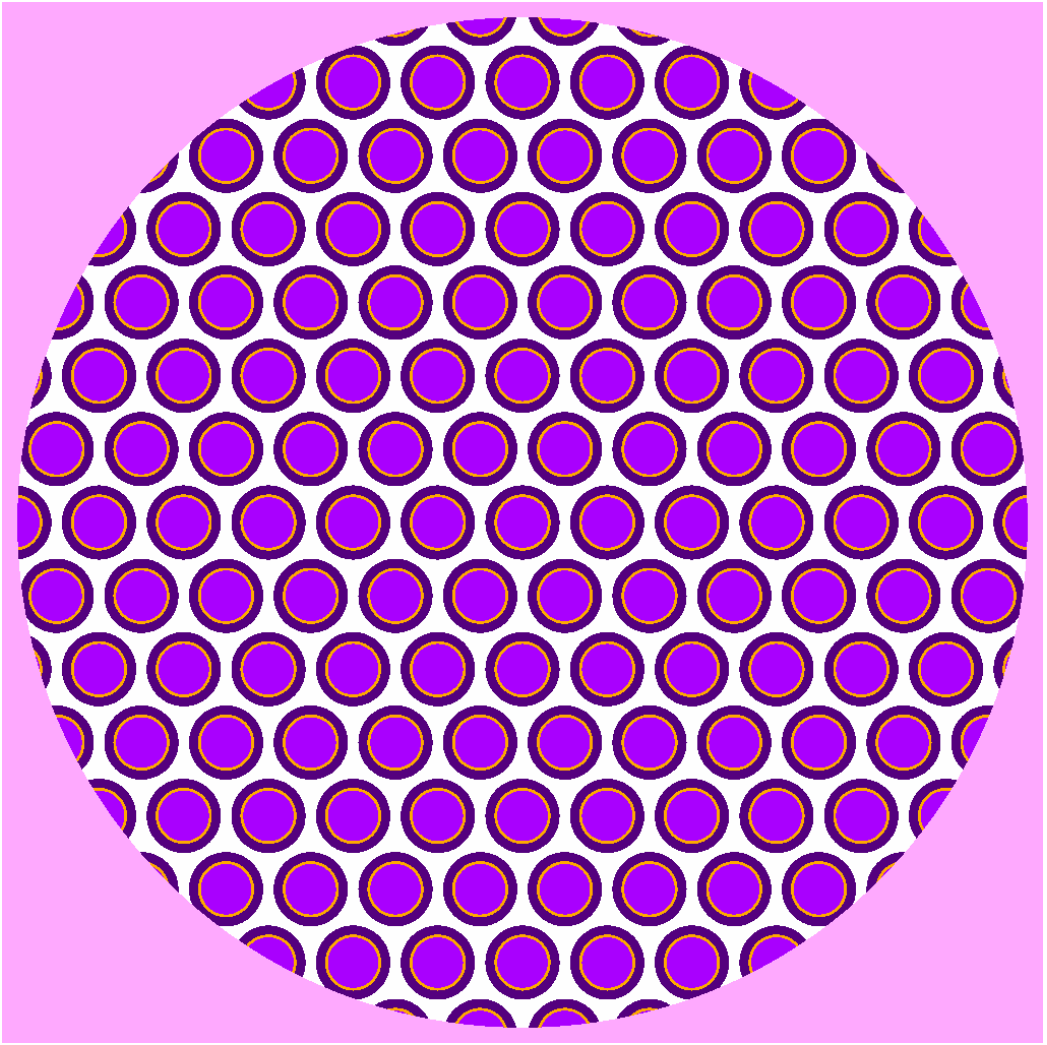


Heterogeneous
Multiscale model

- Distinct models are combined on different length scales into a single (relatively efficient) Monte Carlo simulation

HetMS microscopic scoring volume



HetMS microscopic scoring volume

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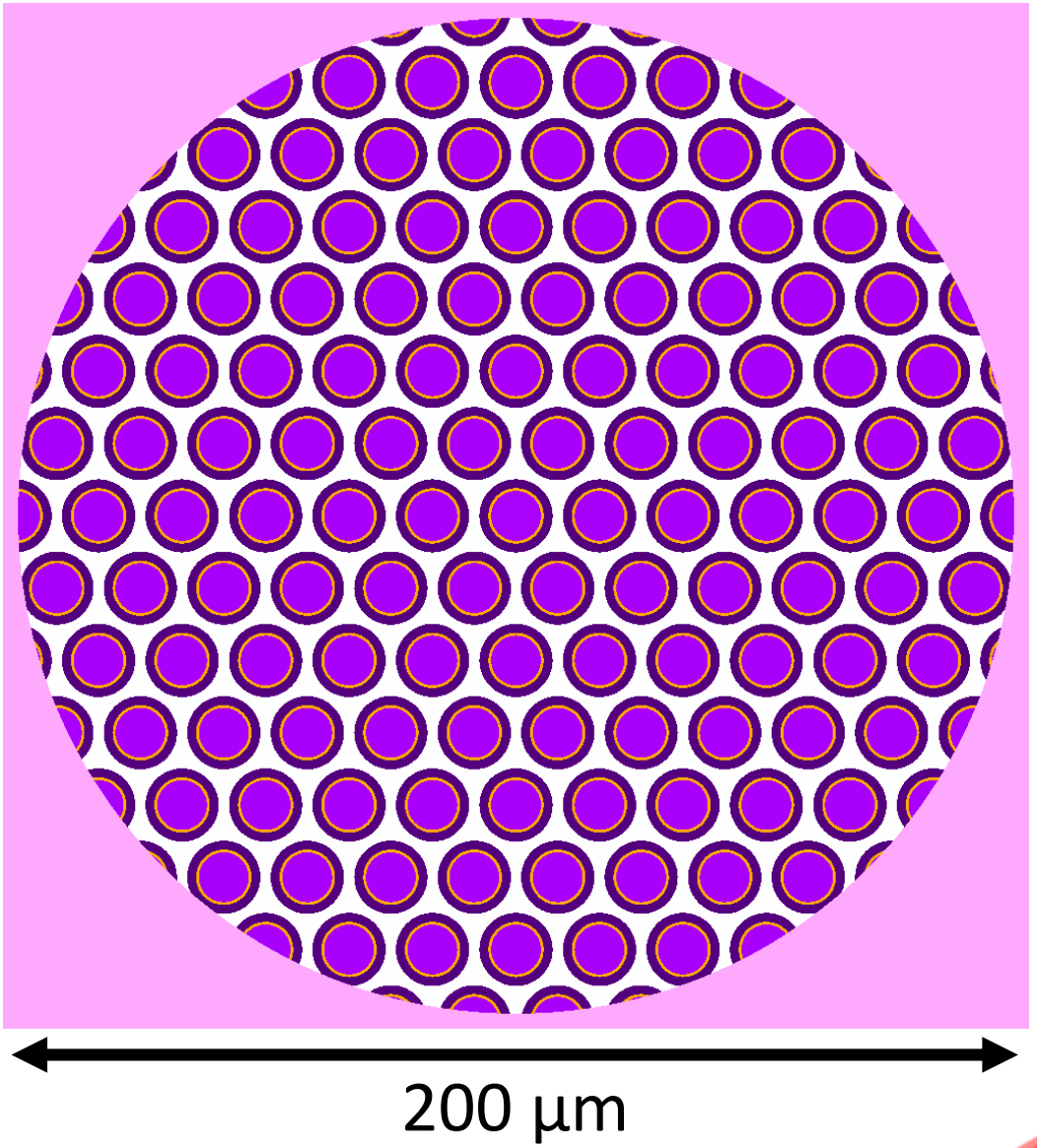

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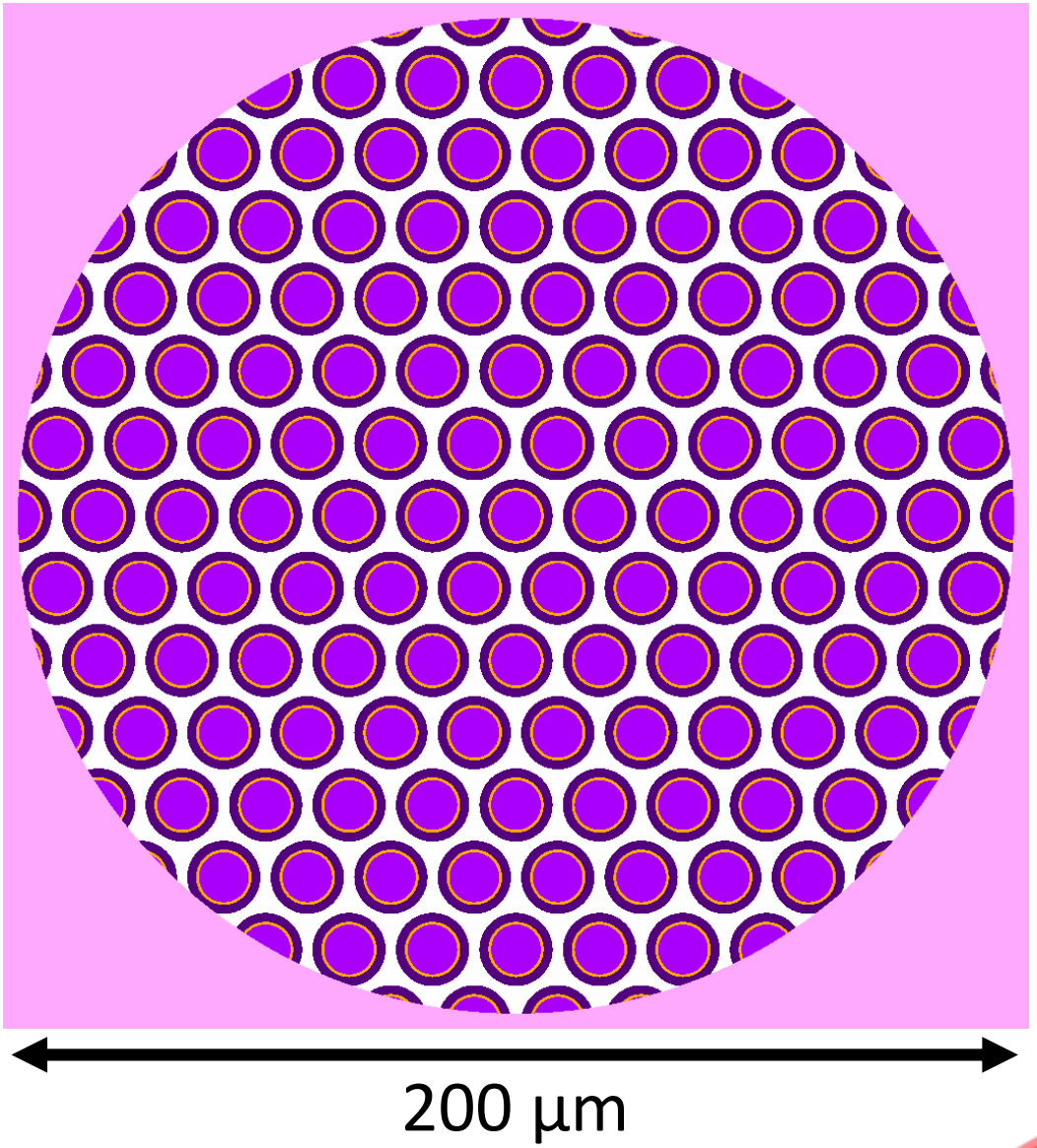

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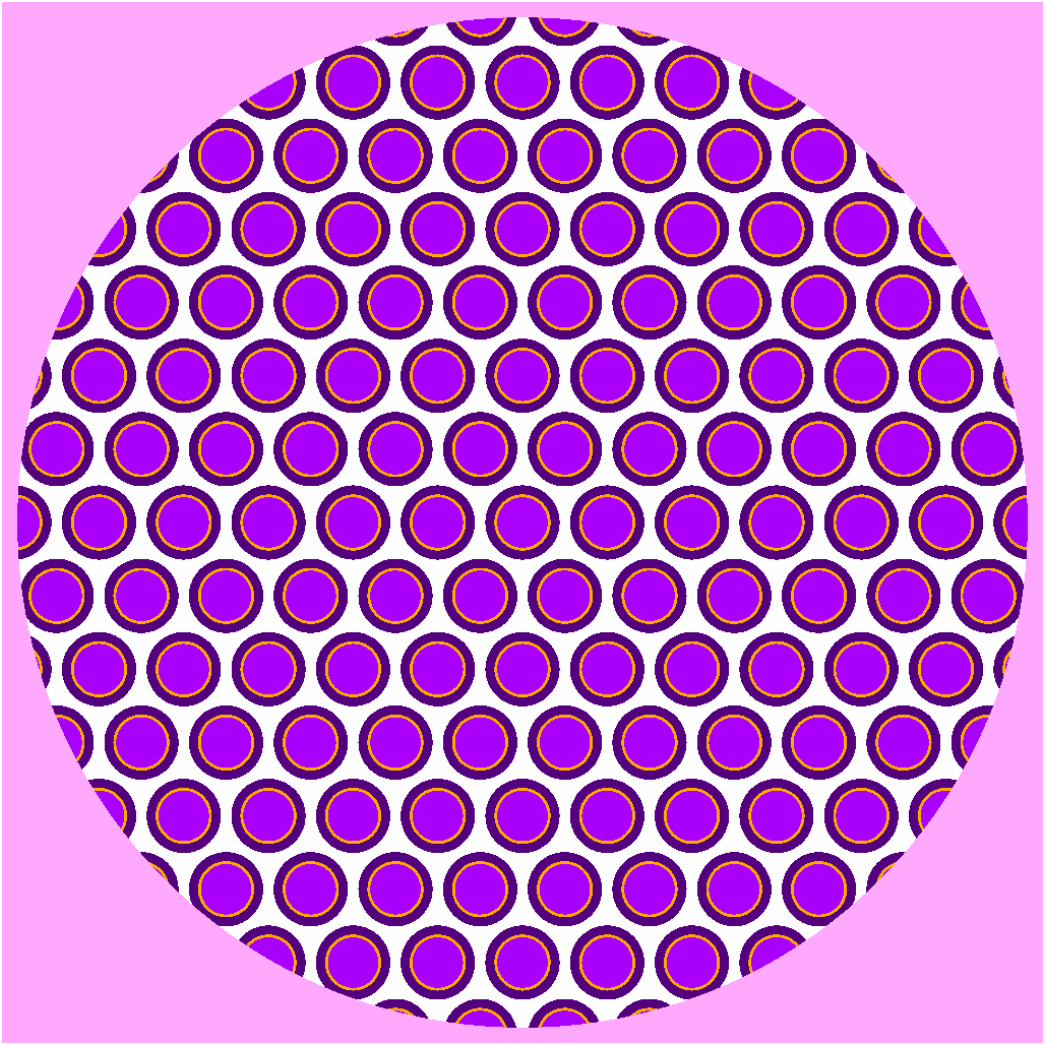

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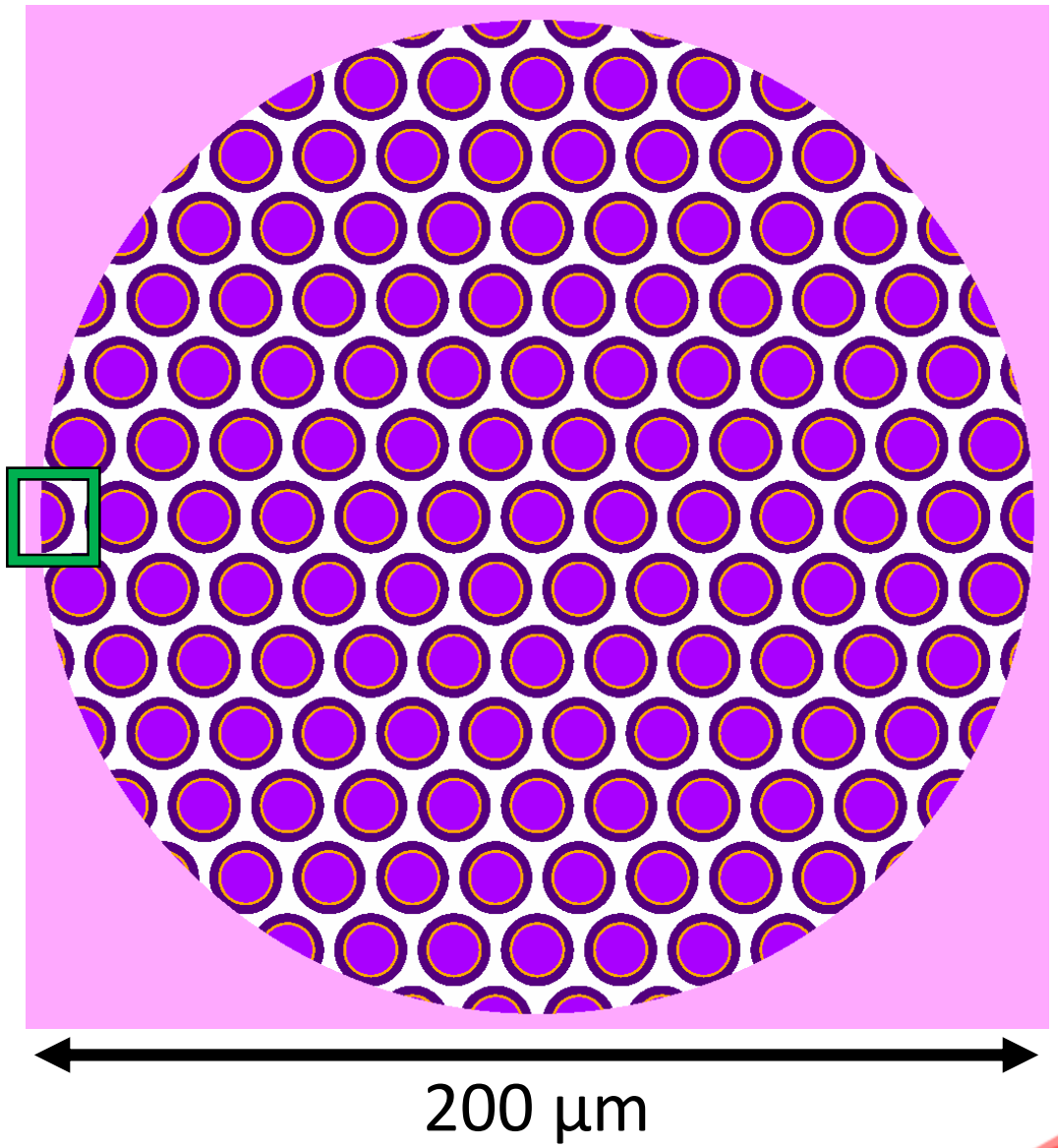
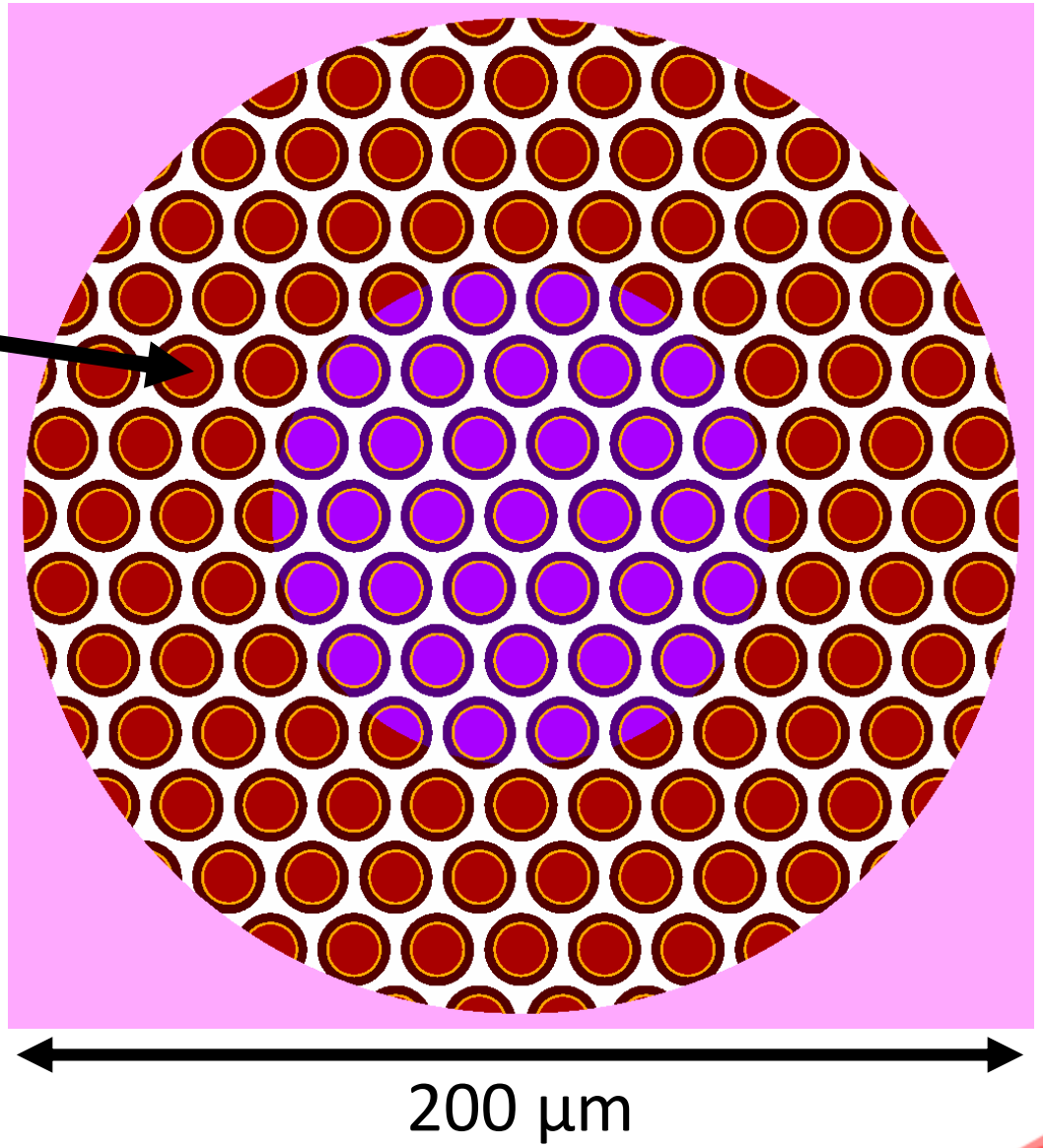


HetMS microscopic scoring volume

non-scoring
buffer cells



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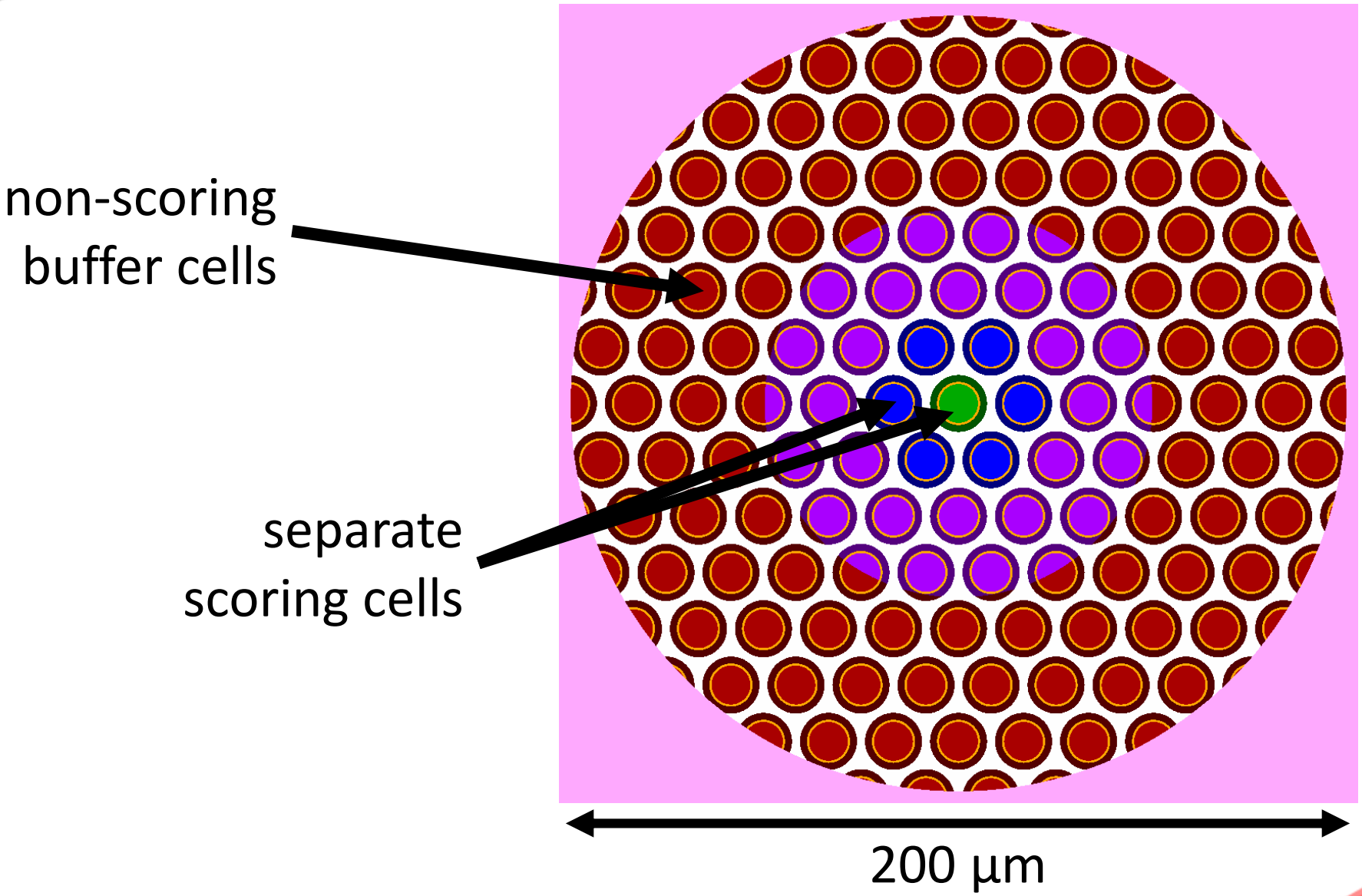

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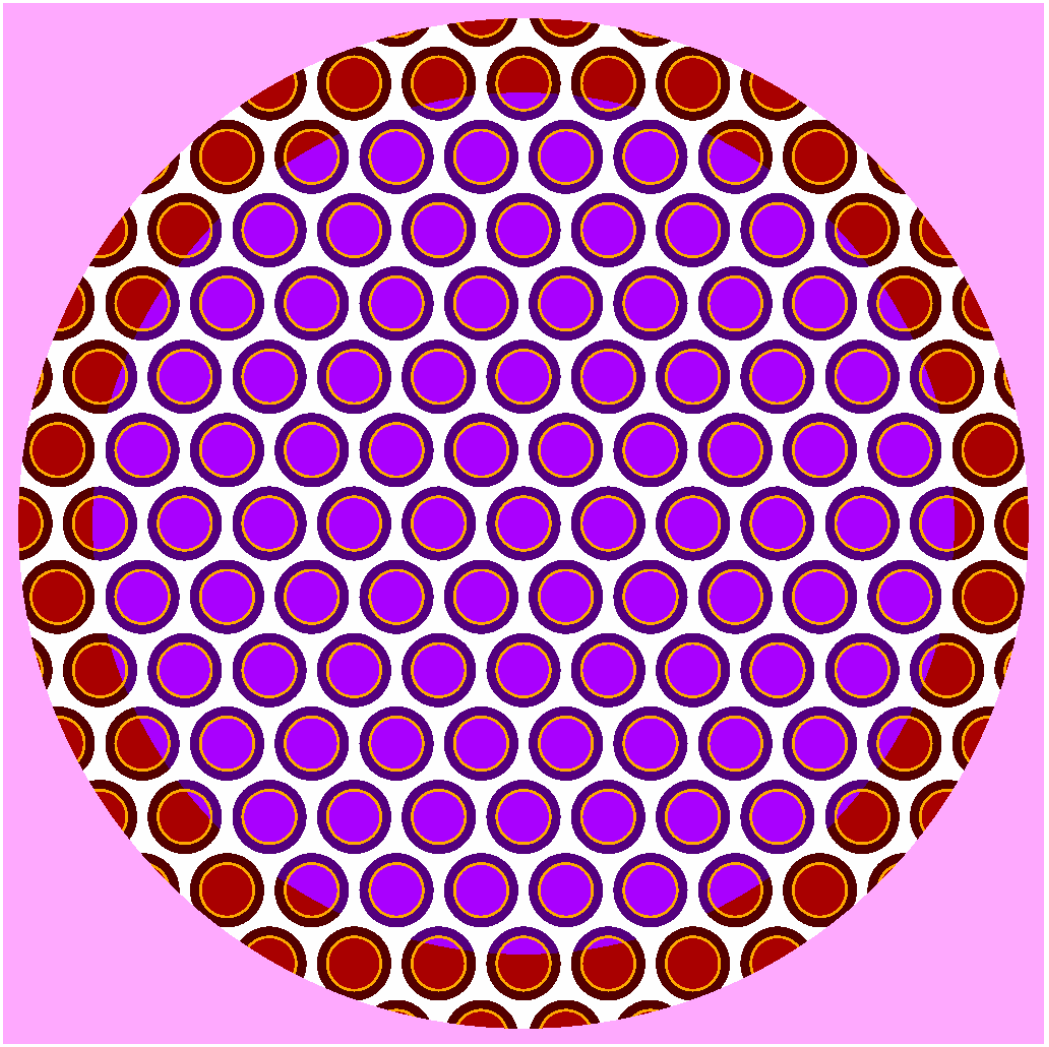

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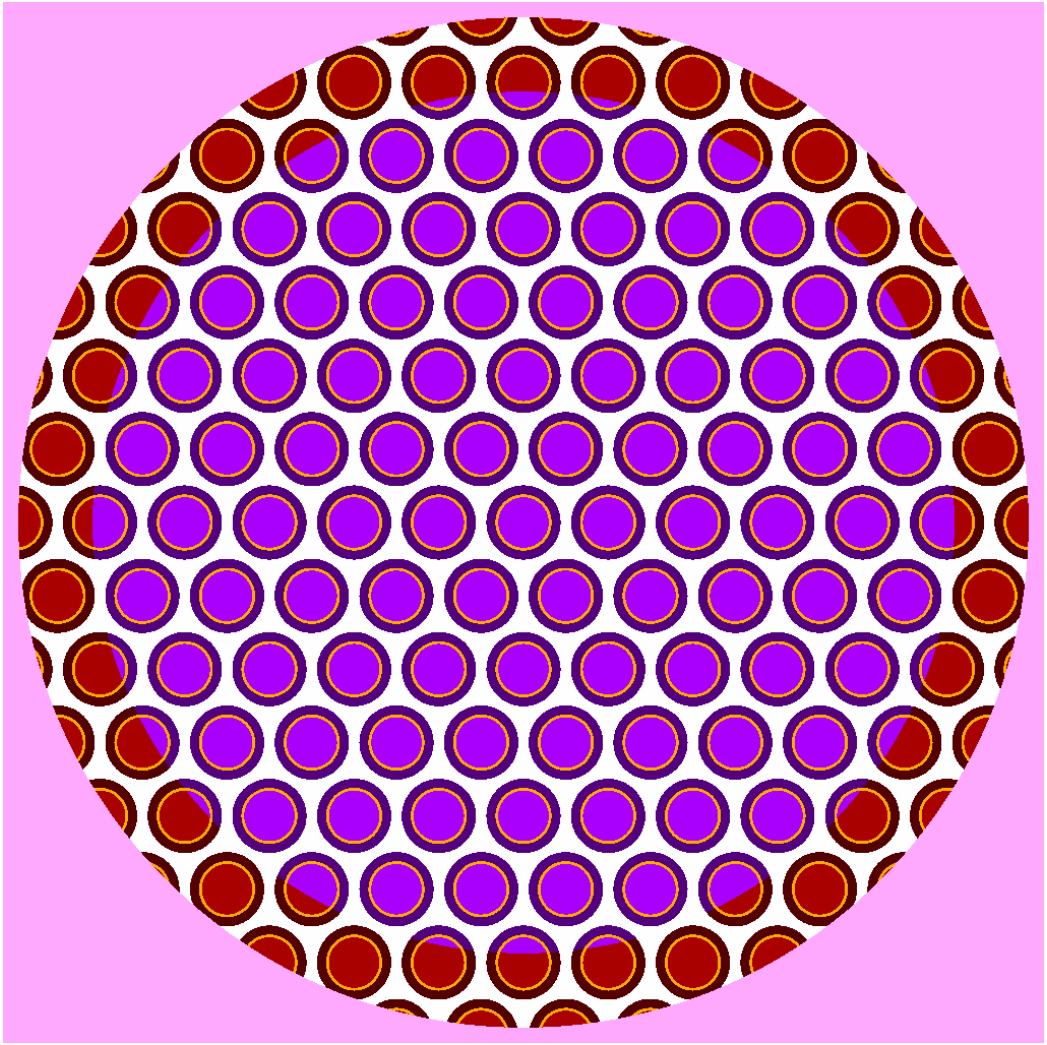
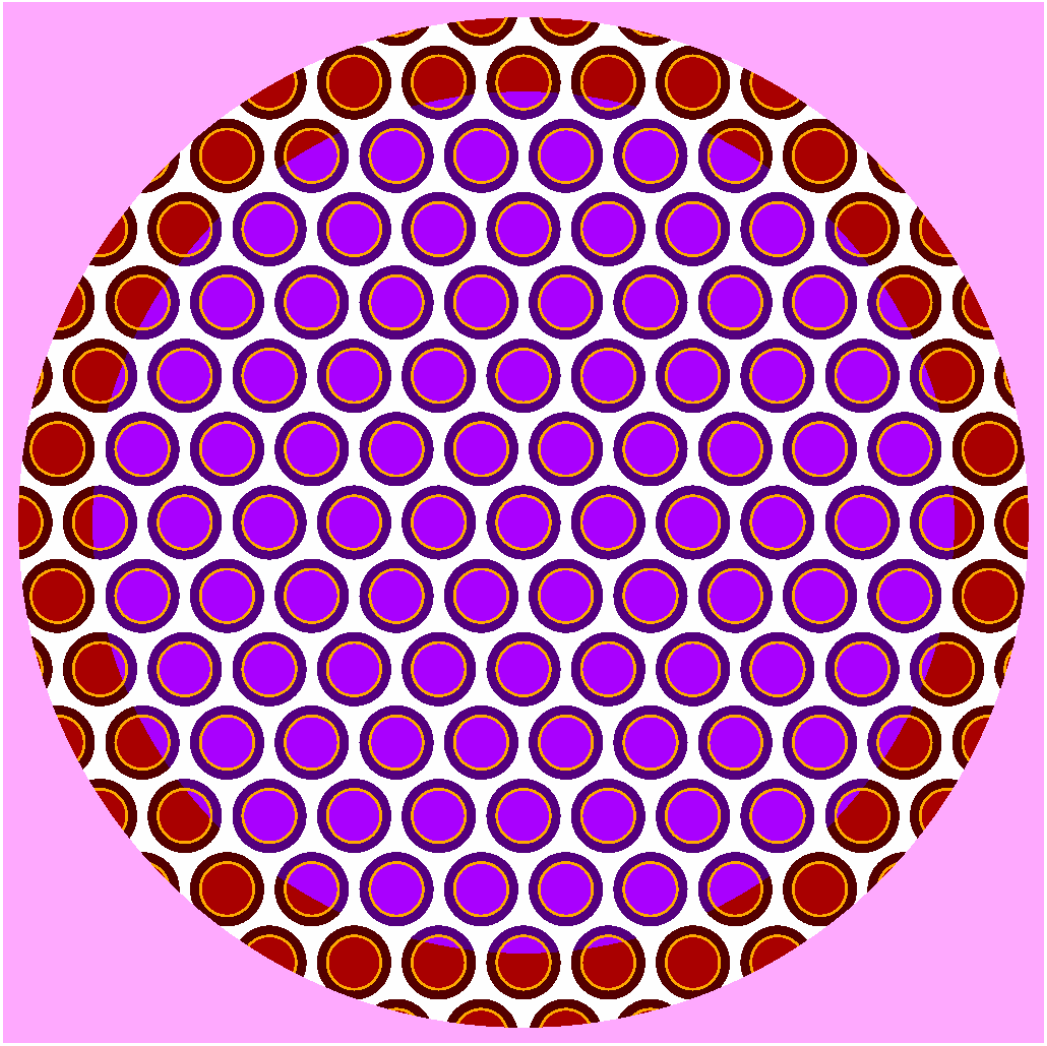


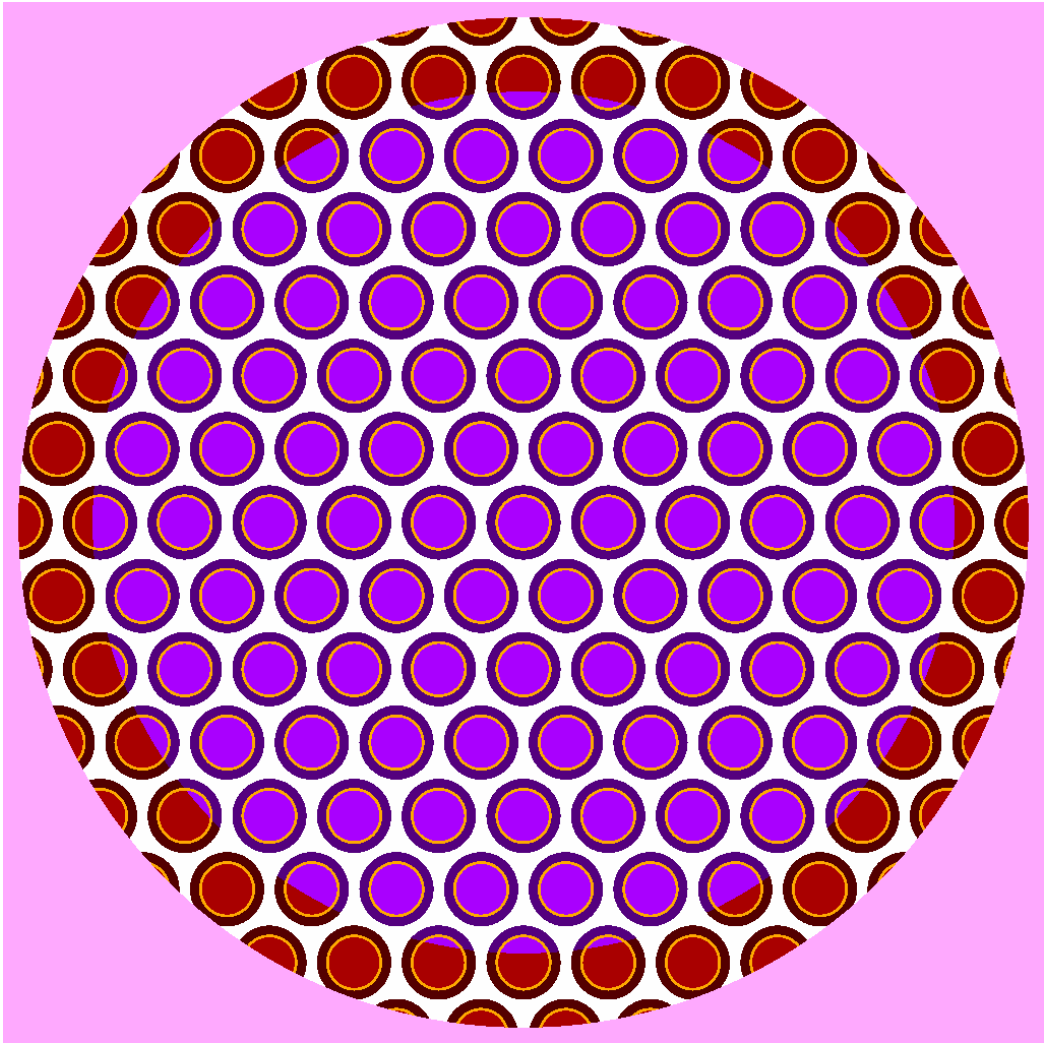
HetMS microscopic scoring volume

- Cells are not sensitive to gold concentration variations in neighbours
- Scoring volume size enhances efficiency

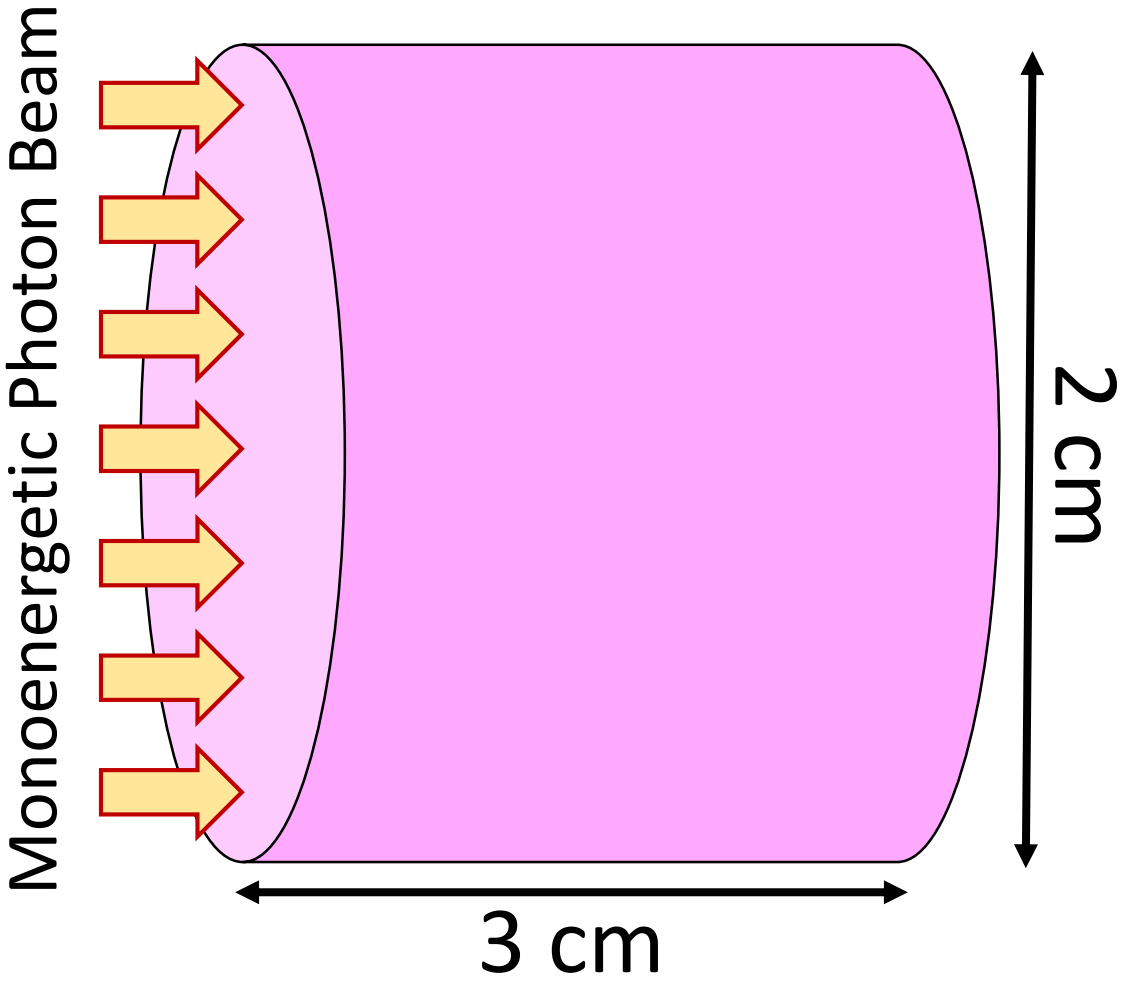


HetMS microscopic scoring volume

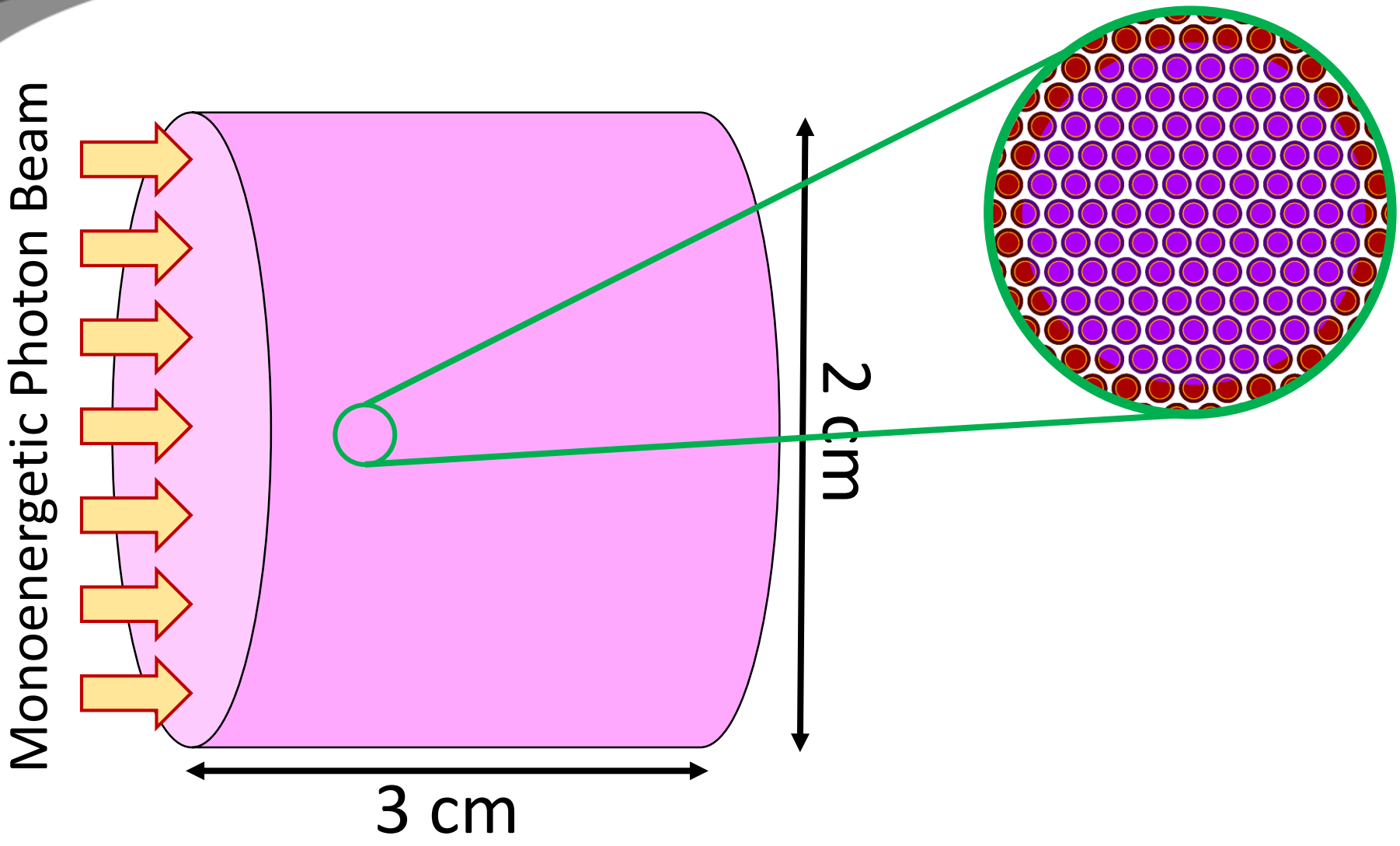
- Cells are not sensitive to gold concentration variations in neighbours
- Scoring volume size enhances efficiency
- The lattice is rotated to not be parallel to the source



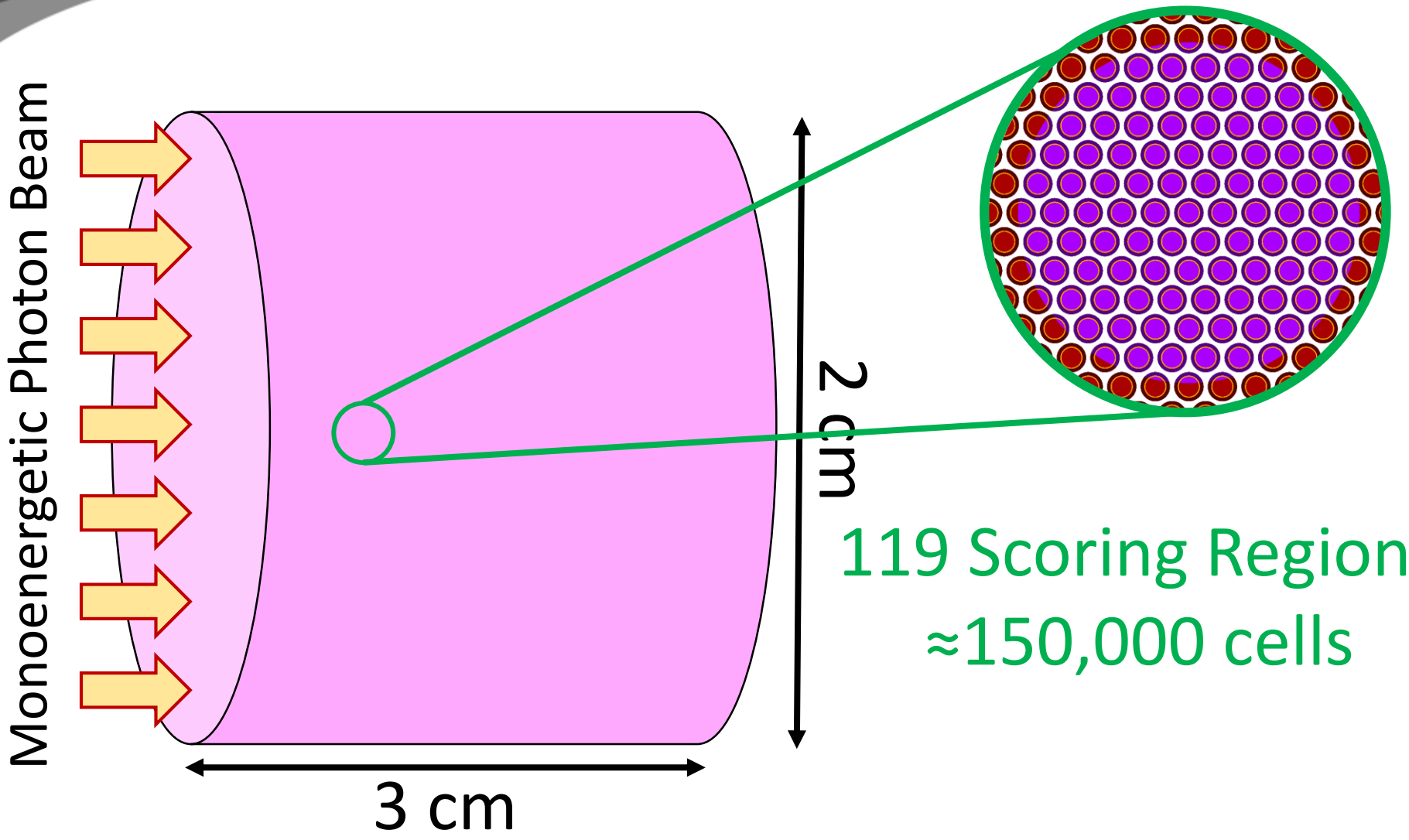
HetMS full model



HetMS full model



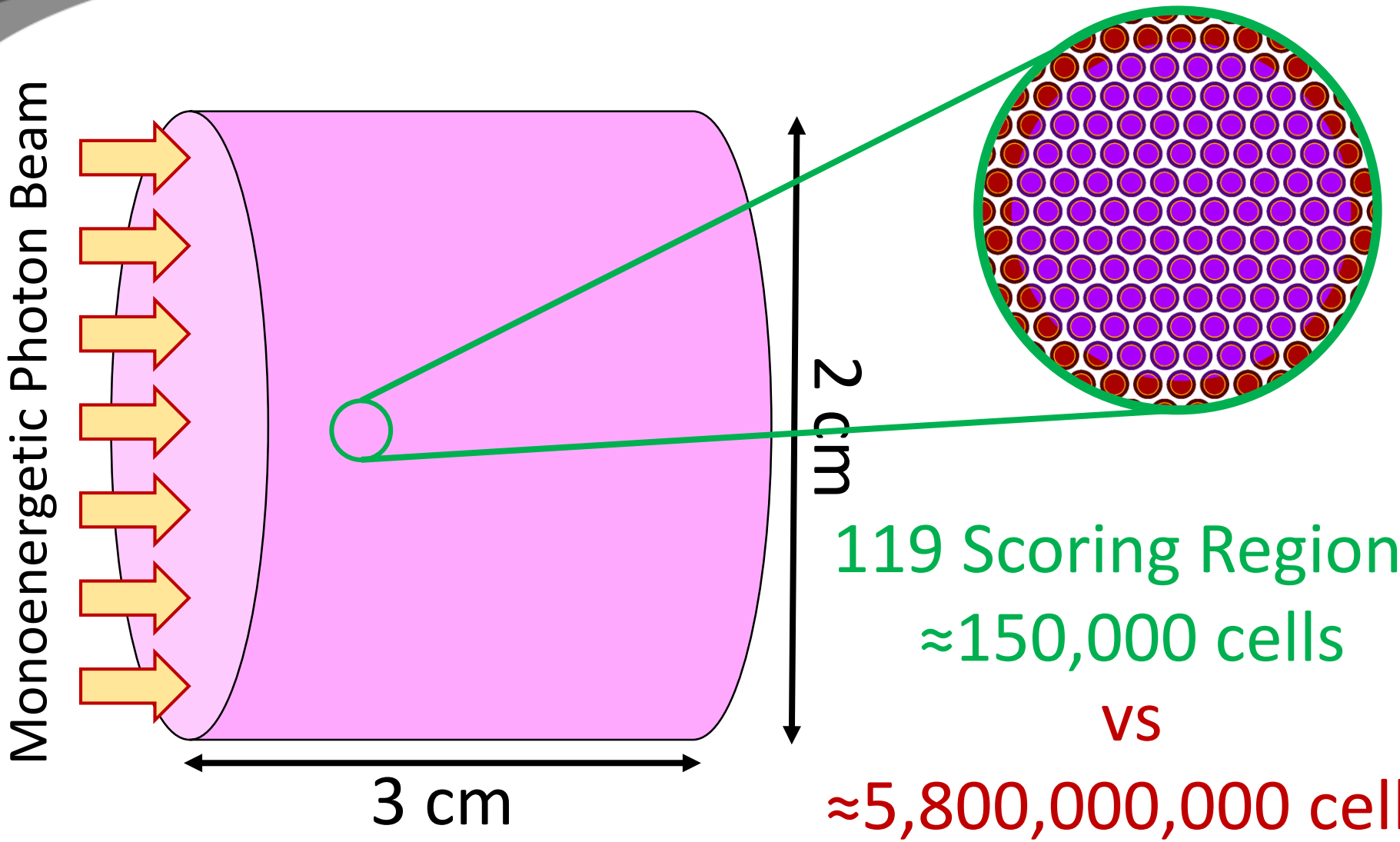
HetMS full model



119 Scoring Regions

≈150,000 cells

HetMS full model



119 Scoring Regions

≈150,000 cells

vs

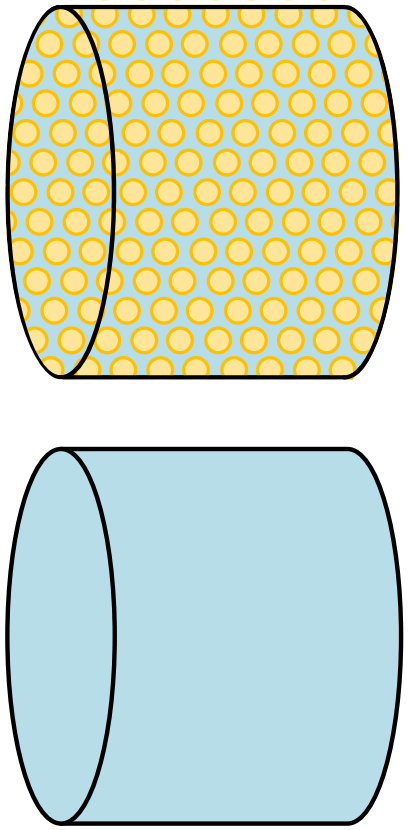
≈5,800,000,000 cells

Scatter phantom

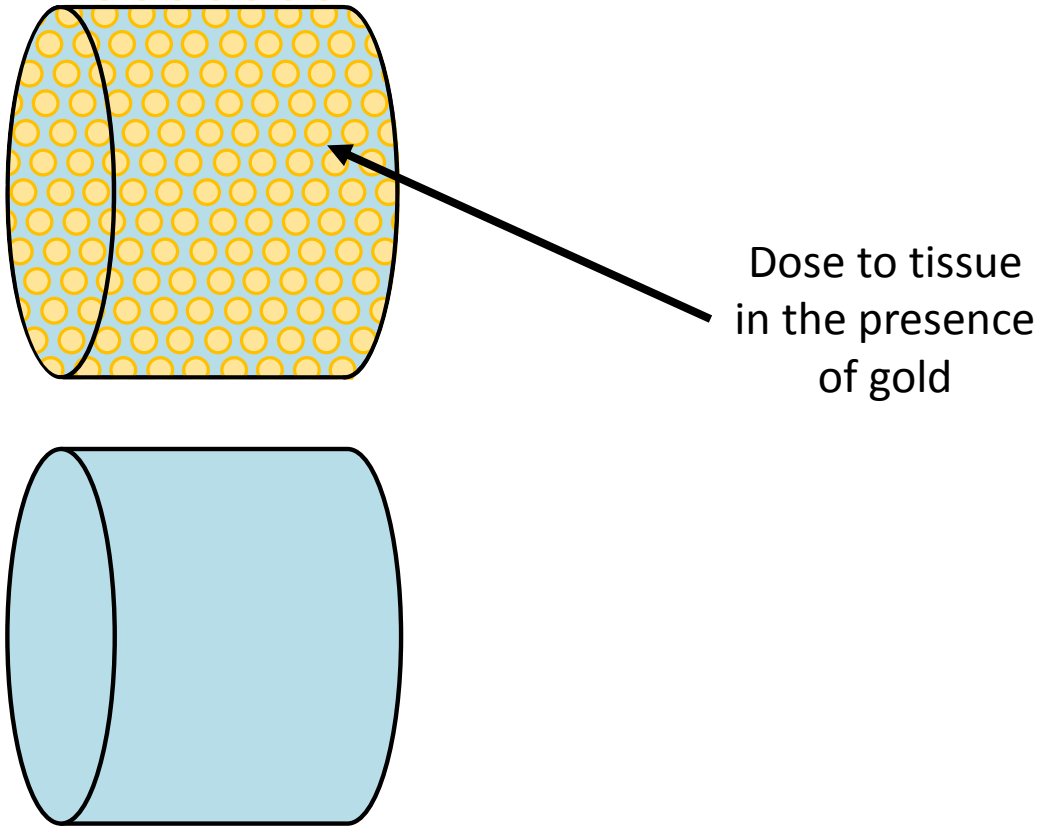
Overview

- Modelling cell and GNP geometry
- Heterogeneous Multiscale Model
  - Introduction
  - Creating a scoring volume
  - Full phantom model
- Results

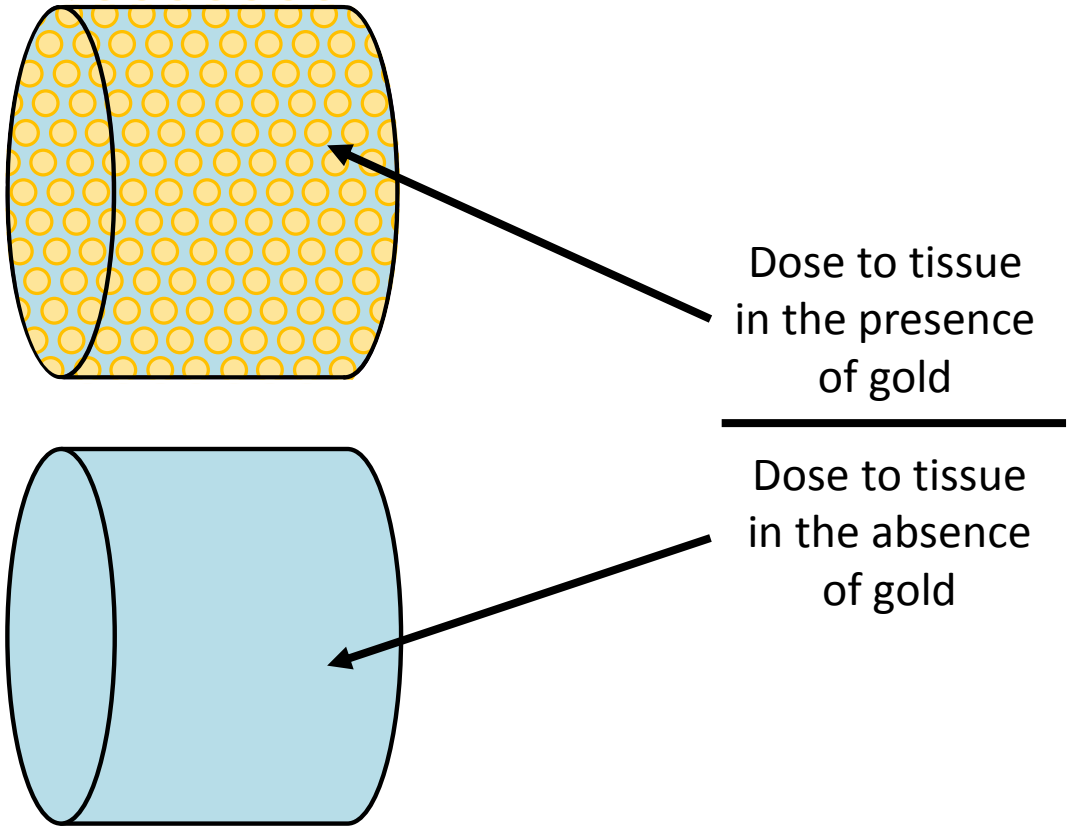
Dose **E**nhancement **F**actor (DEF)



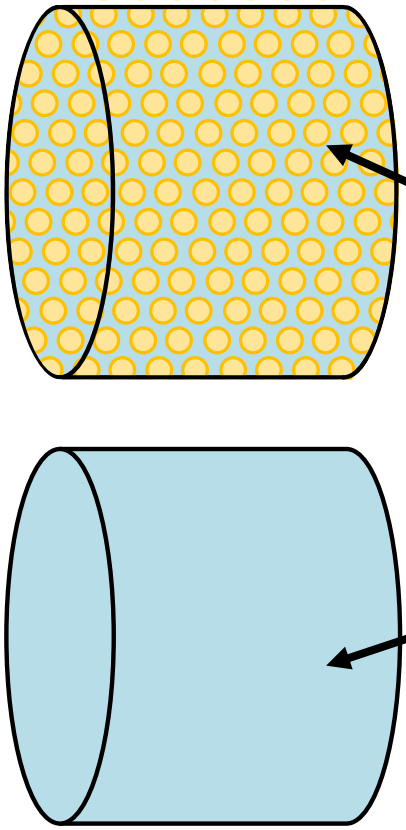
Dose Enhancement Factor (DEF)



Dose Enhancement Factor (DEF)



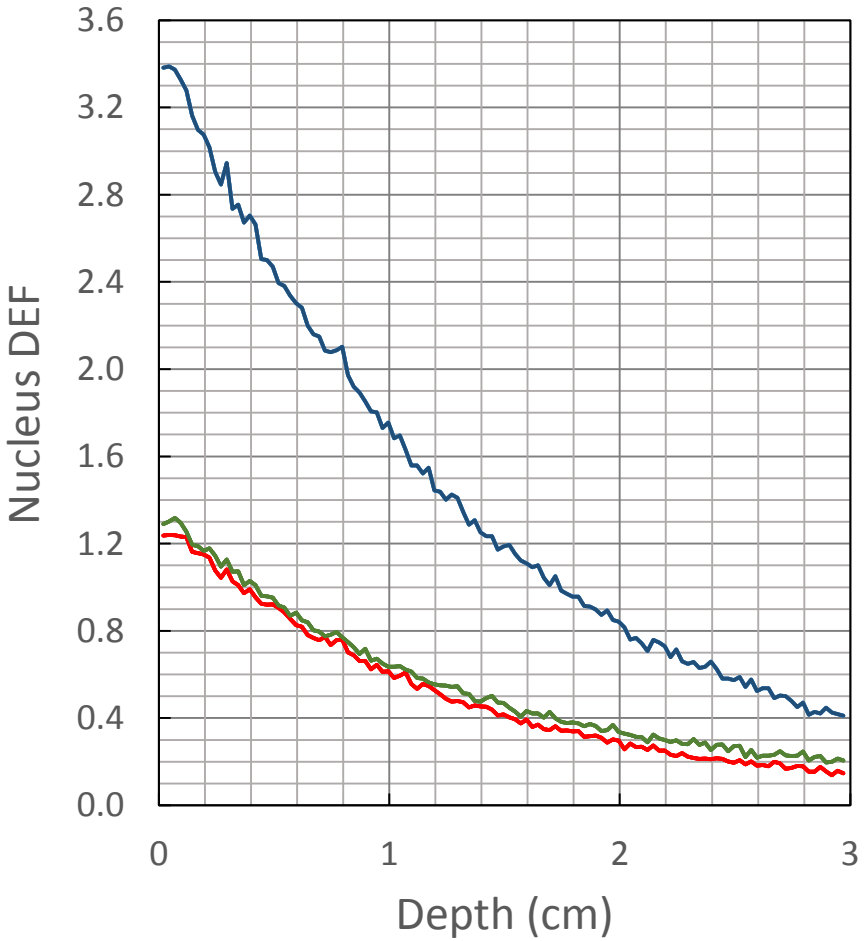
Dose Enhancement Factor (DEF)

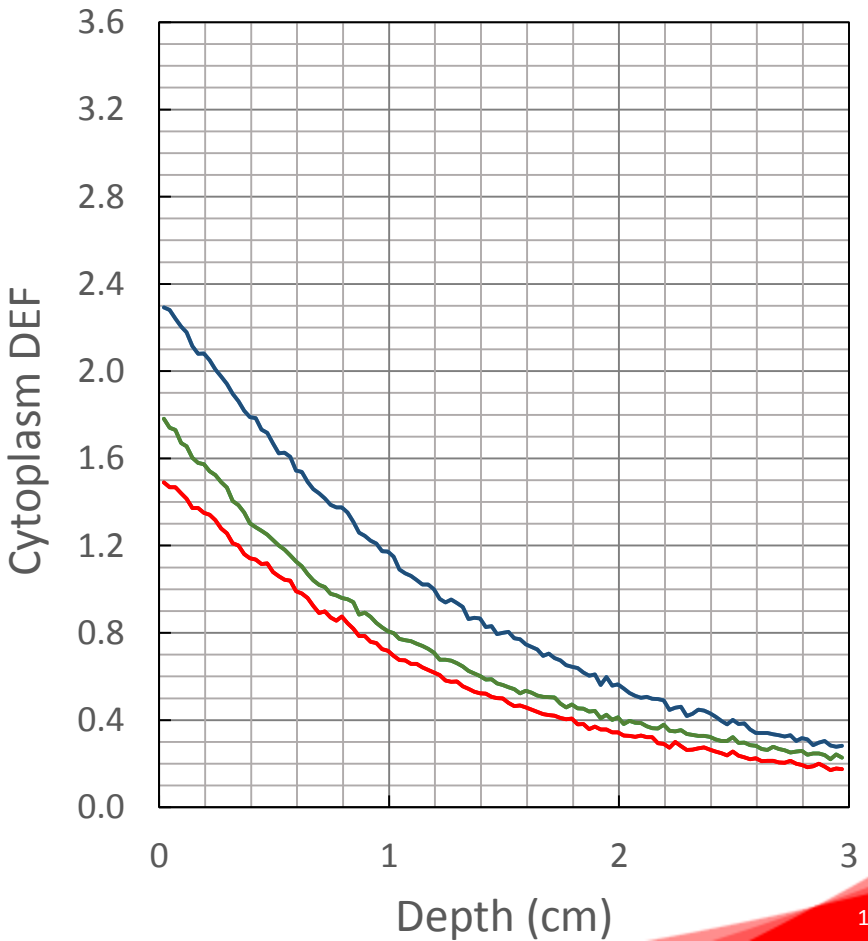


$$\frac{\text{Dose to tissue in the presence of gold}}{\text{Dose to tissue in the absence of gold}} = \text{DEF}$$

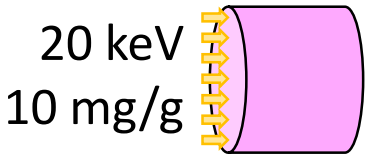
DEF vs Depth

20 keV
10 mg/g

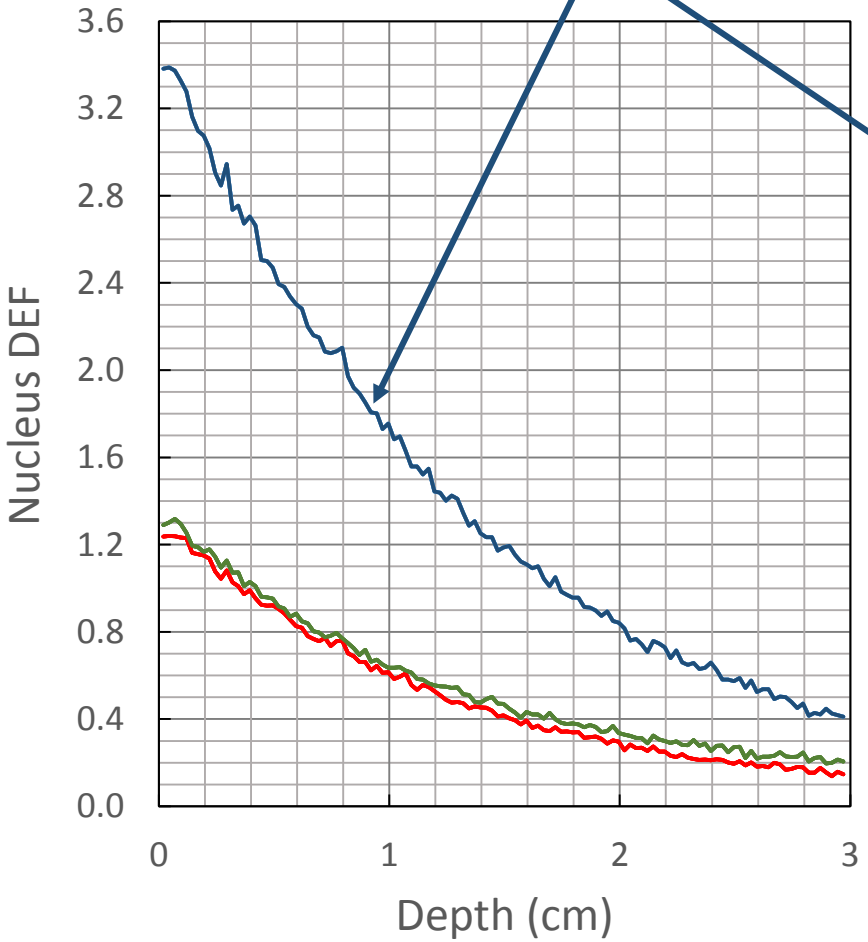


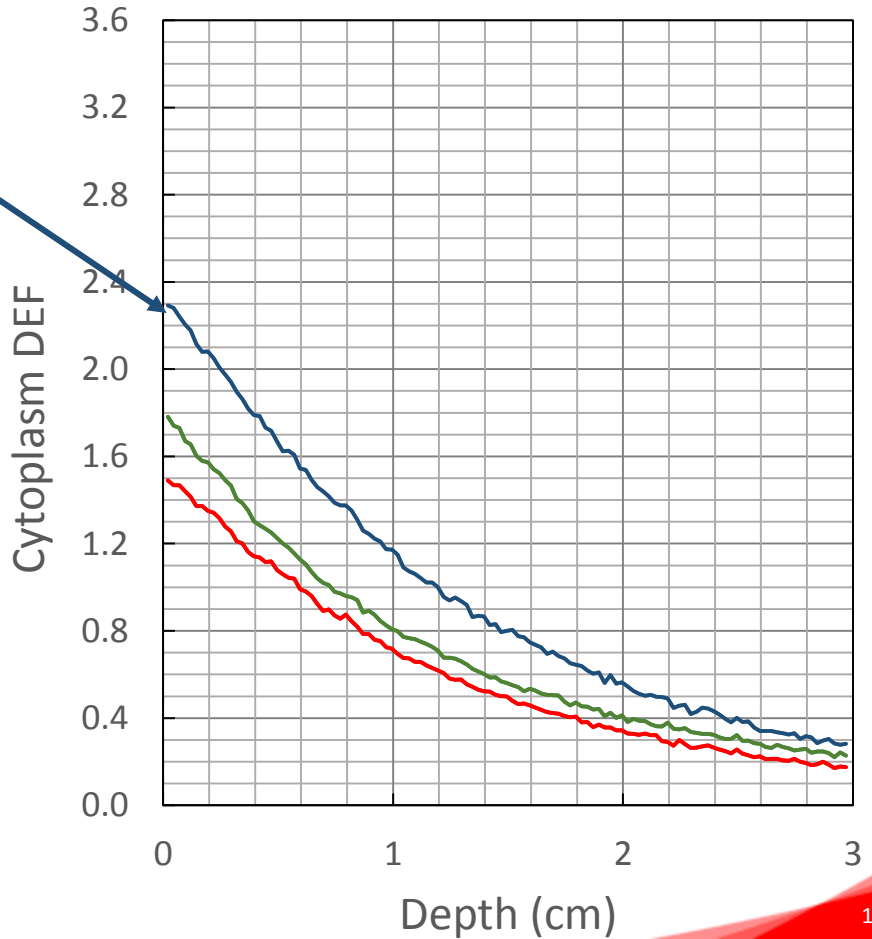


DEF vs Depth

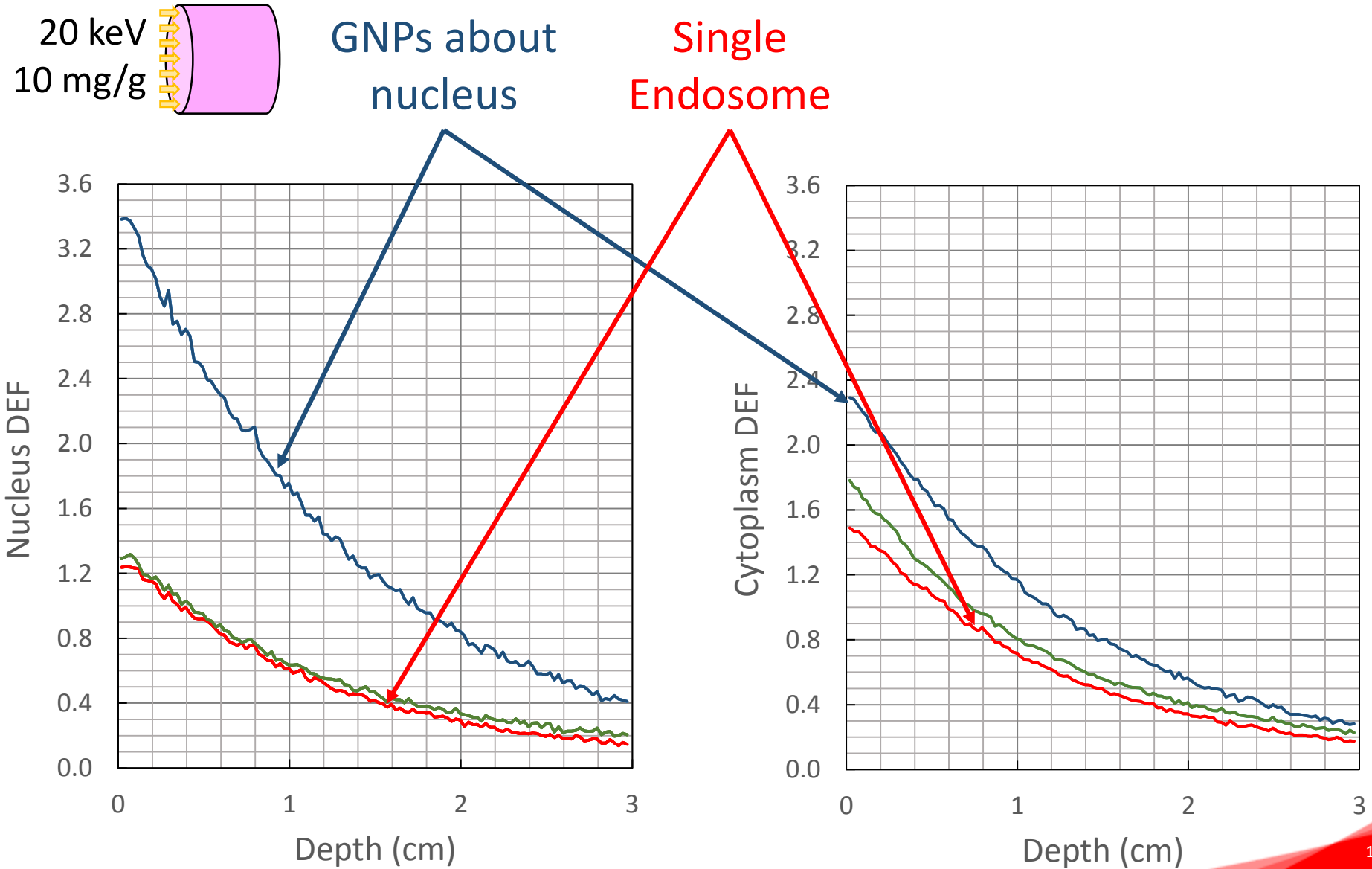


GNPs about nucleus

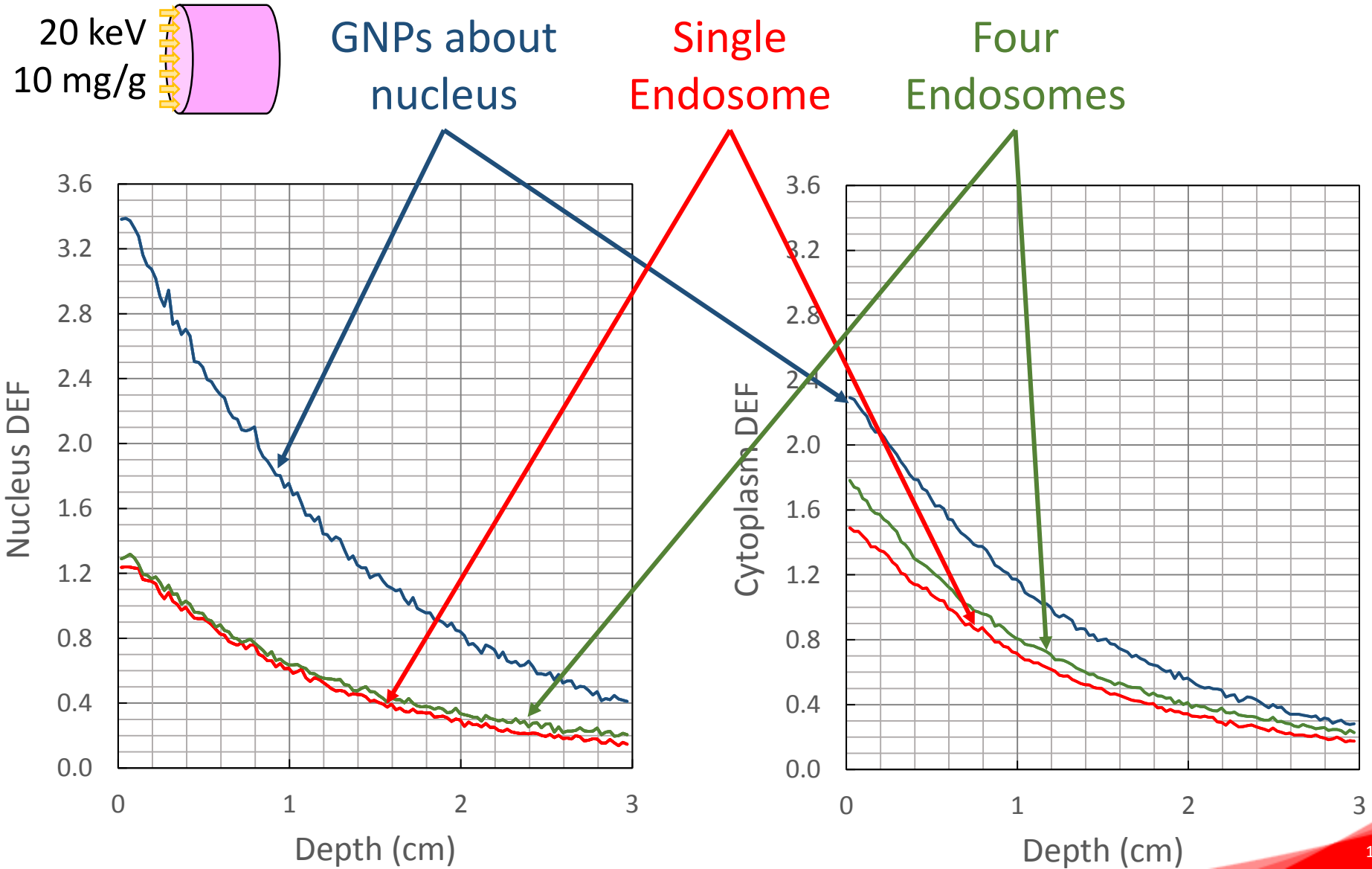




DEF vs Depth

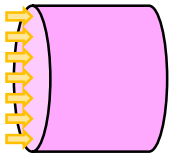

20 keV
10 mg/g
GNPs about nucleus
Single Endosome
Nucleus DEF
Cytoplasm DEF
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
0
1
2
3
Depth (cm)
Depth (cm)

DEF vs Depth


20 keV
10 mg/g
GNPs about nucleus
Single Endosome
Four Endosomes
Nucleus DEF
Cytoplasm DEF
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
0
1
2
3
Depth (cm)
Depth (cm)

DEF vs Depth

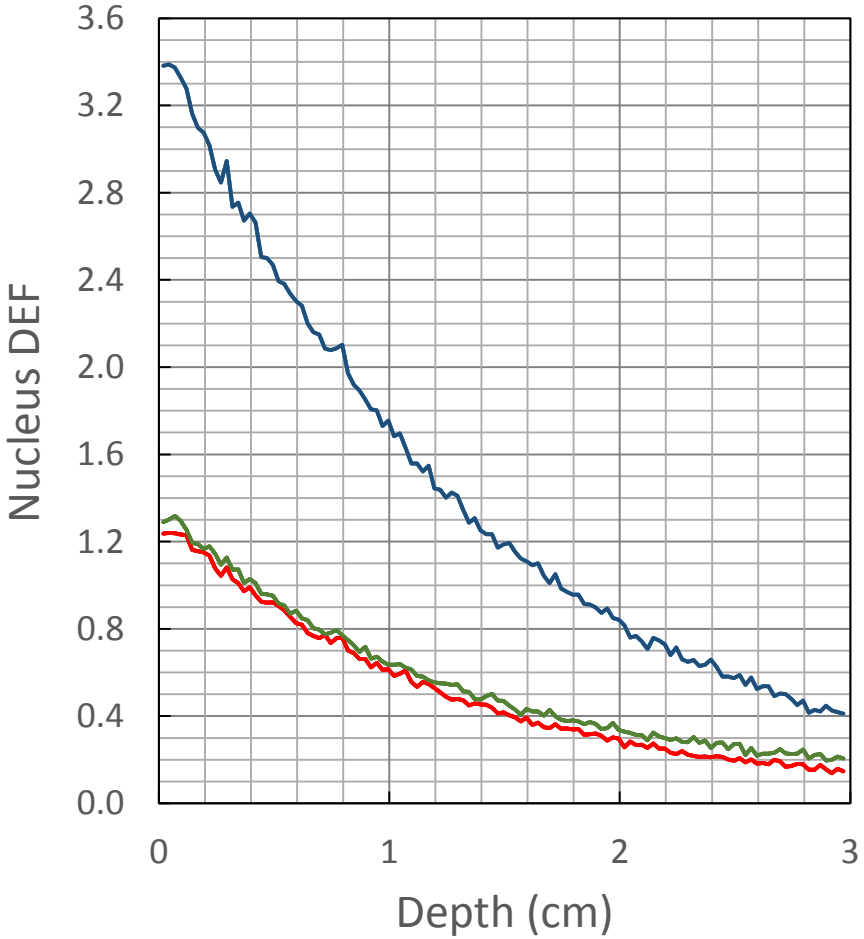
20 keV
10 mg/g



GNPs about nucleus

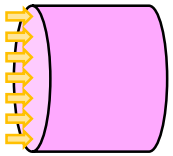
Single Endosome

Four Endosomes



DEF vs Depth

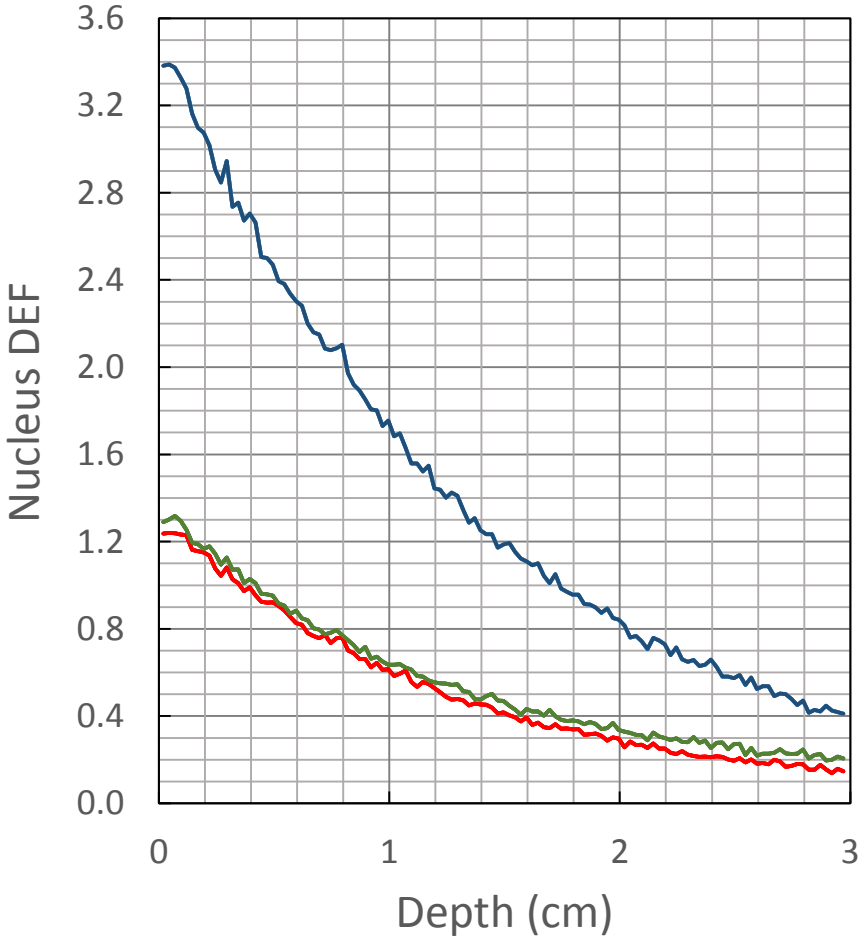
20 keV
10 mg/g



GNPs about nucleus

Single Endosome

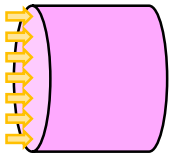
Four Endosomes



- DEF is highest when GNPs gather about the nucleus

DEF vs Depth

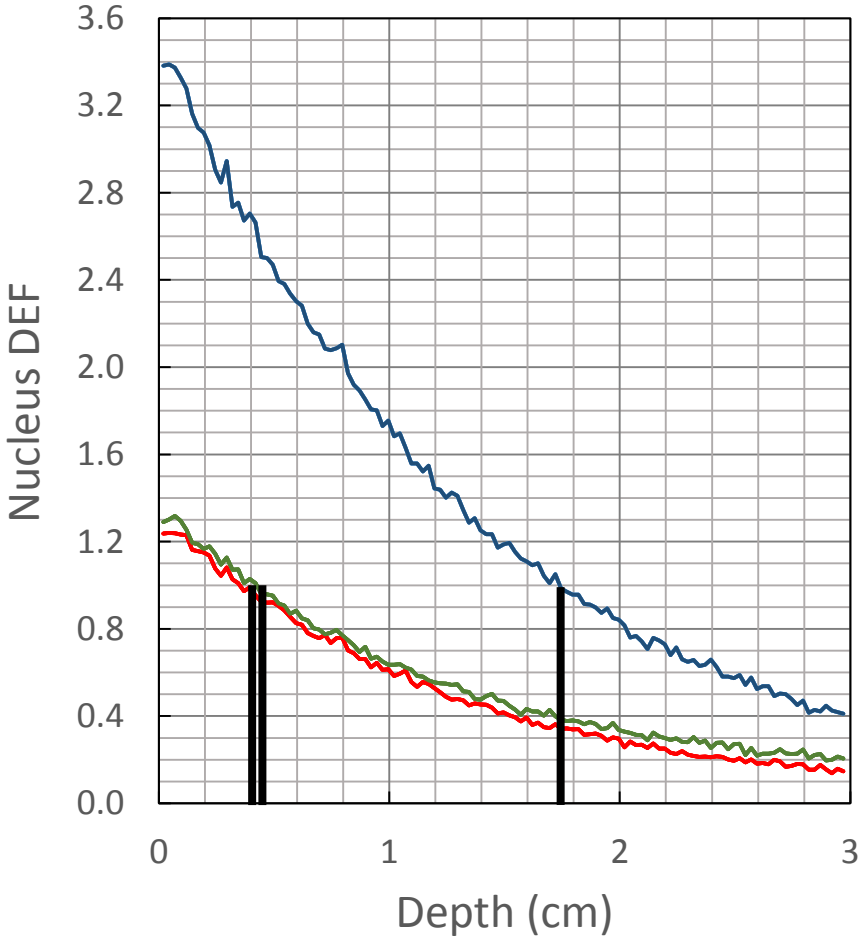
20 keV
10 mg/g



GNPs about nucleus

Single Endosome

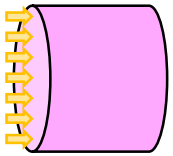
Four Endosomes



- DEF is highest when GNPs gather about the nucleus
- DEF drops below 1 at various depths within the phantom

DEF vs Depth

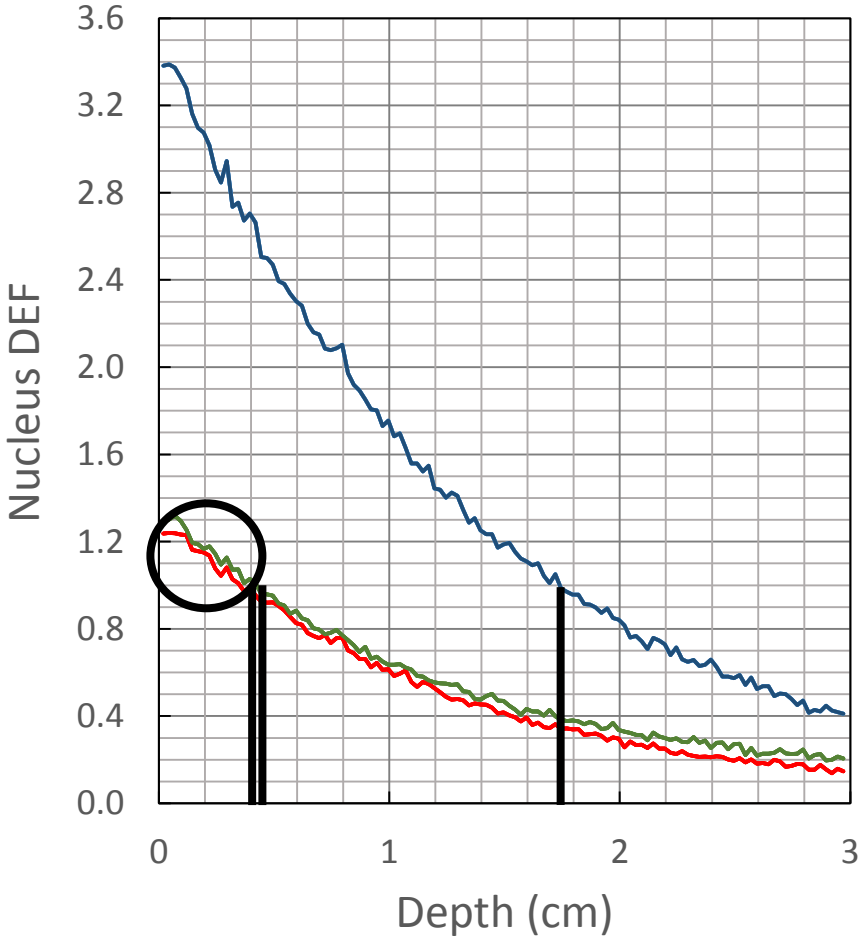
20 keV
10 mg/g



GNPs about nucleus

Single Endosome

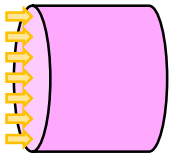
Four Endosomes



- DEF is highest when GNPs gather about the nucleus
- DEF drops below 1 at various depths within the phantom
- Low nucleus DEFs for GNPs in endosomes

DEF vs Depth

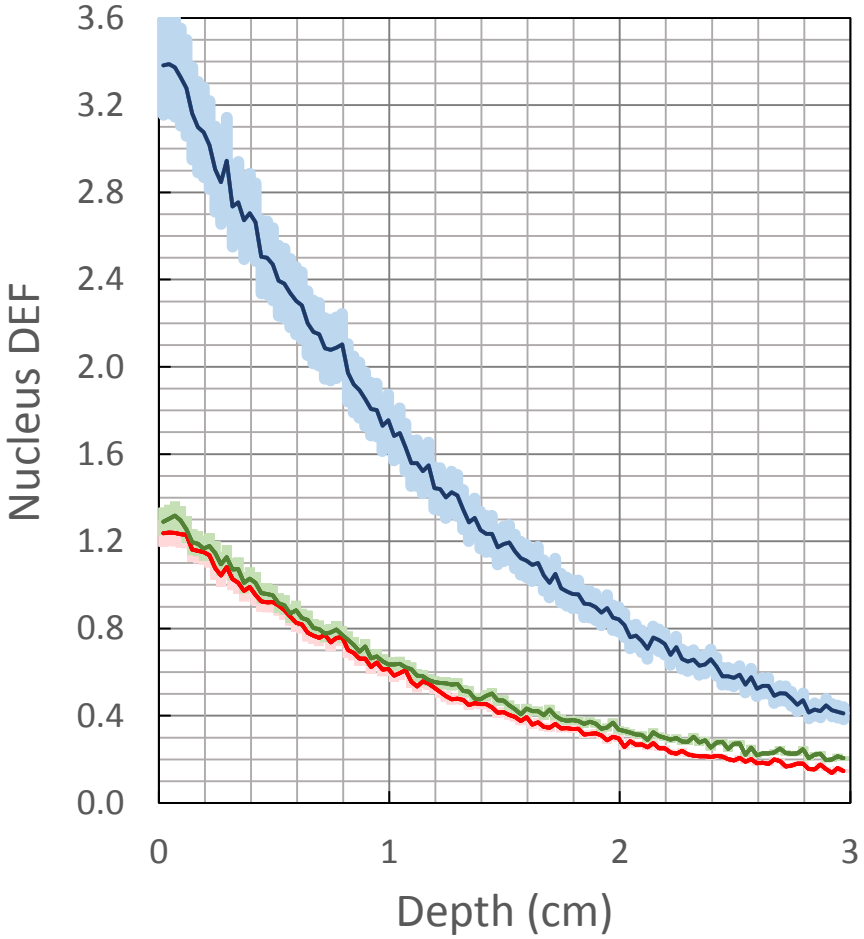
20 keV
10 mg/g



GNPs about nucleus

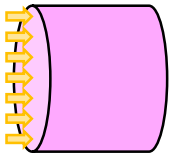
Single Endosome

Four Endosomes



- Shaded region represents a local 10% variation in gold concentration

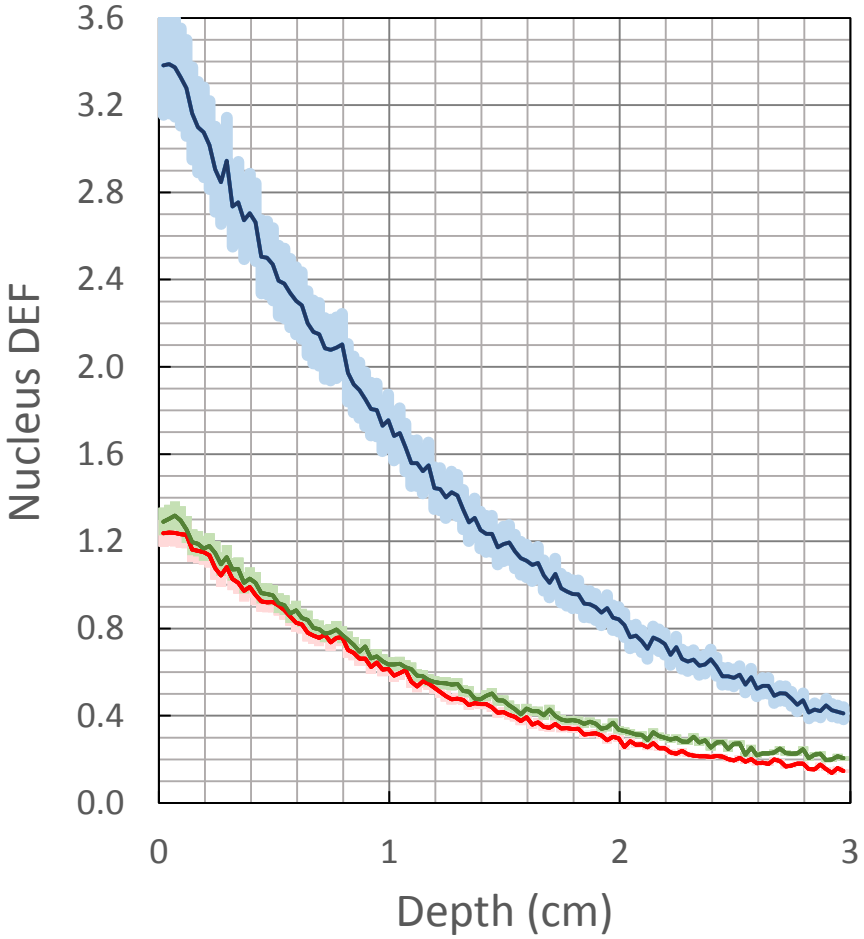
DEF vs Depth



GNPs about nucleus

Single Endosome

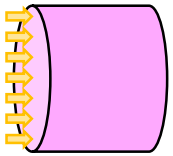
Four Endosomes



- Shaded region represents a local 10% variation in gold concentration
- Simulations are ≈100 times faster using HetMS rather than full cell simulations

DEF vs Depth

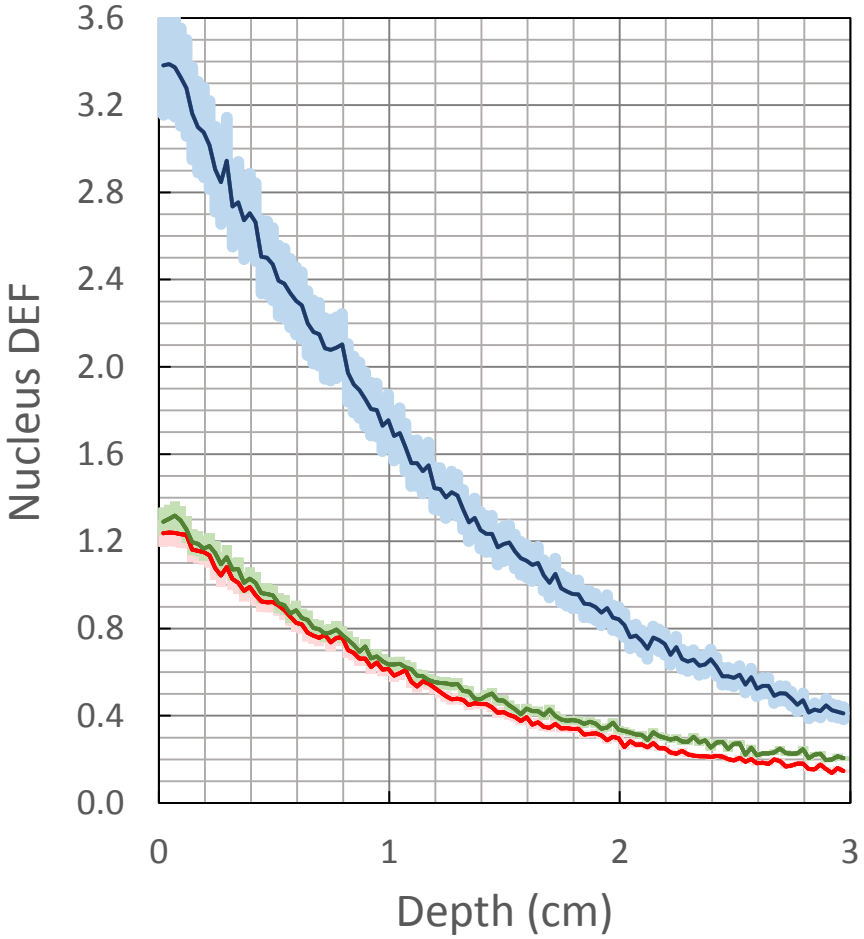
20 keV
10 mg/g



GNPs about nucleus

Single Endosome

Four Endosomes



- Shaded region represents a local 10% variation in gold concentration
- Simulations are ≈100 times faster using HetMS rather than full cell simulations
- Simulations can be up to ≈1000 times faster in the worst case scenarios

Conclusion

- The Heterogeneous Multiscale model is useful for large scale simulation of microscopic metrics

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Conclusion

- The Heterogeneous Multiscale model is useful for large scale simulation of microscopic metrics
- In the context of GNPT, cellular dose enhancement due to GNPs varies with depth in tumour
- Future work
  - To create a more realistic model, incorporating recent experimental work
  - Laying out the extensive validation work done on EGSnrc at small length scales

Acknowledgements

Support from: