Coupled CFD-PBE Predictions of Renal Stone Size Distributions in the Nephron in Microgravity

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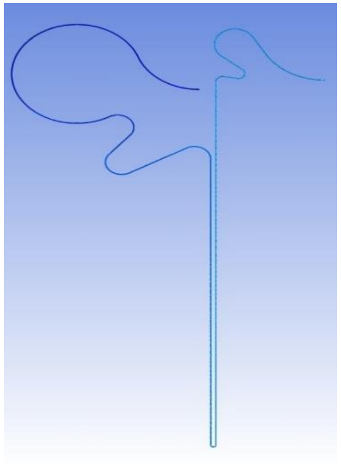
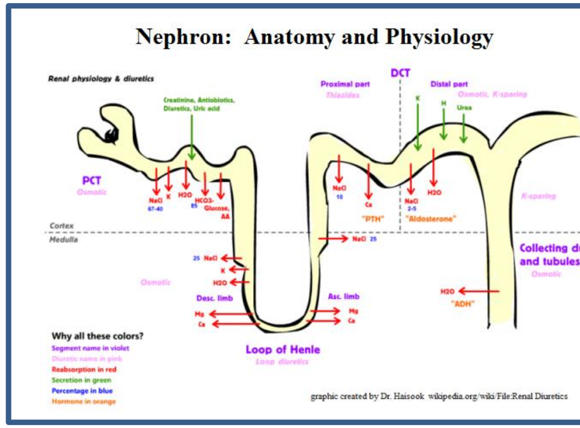
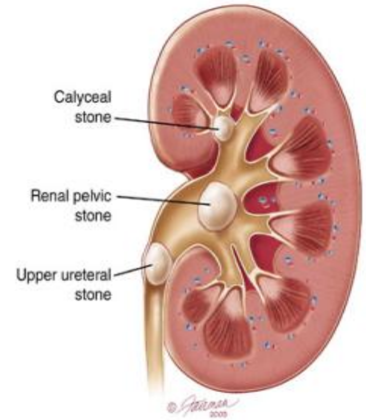
Renal Biochemistry Alteration in Microgravity

- The physiological, environmental and dietary conditions of space travel increase the risk for development of renal stones.
  - Bone atrophy → increased concentration of calcium
  - Dehydration & the lower urine output → reduced urine volumes
  - high sodium and animal protein diet → increased salt - low pH
  - low urinary citrate and magnesium → lack of sufficient stone-forming inhibitors
- These factors all provide favorable conditions for promoting increased crystallization and agglomeration (Whitson, 2010).

System & Multiphase CFD Models for Renal Stone Development & Transport in 1G and Microgravity



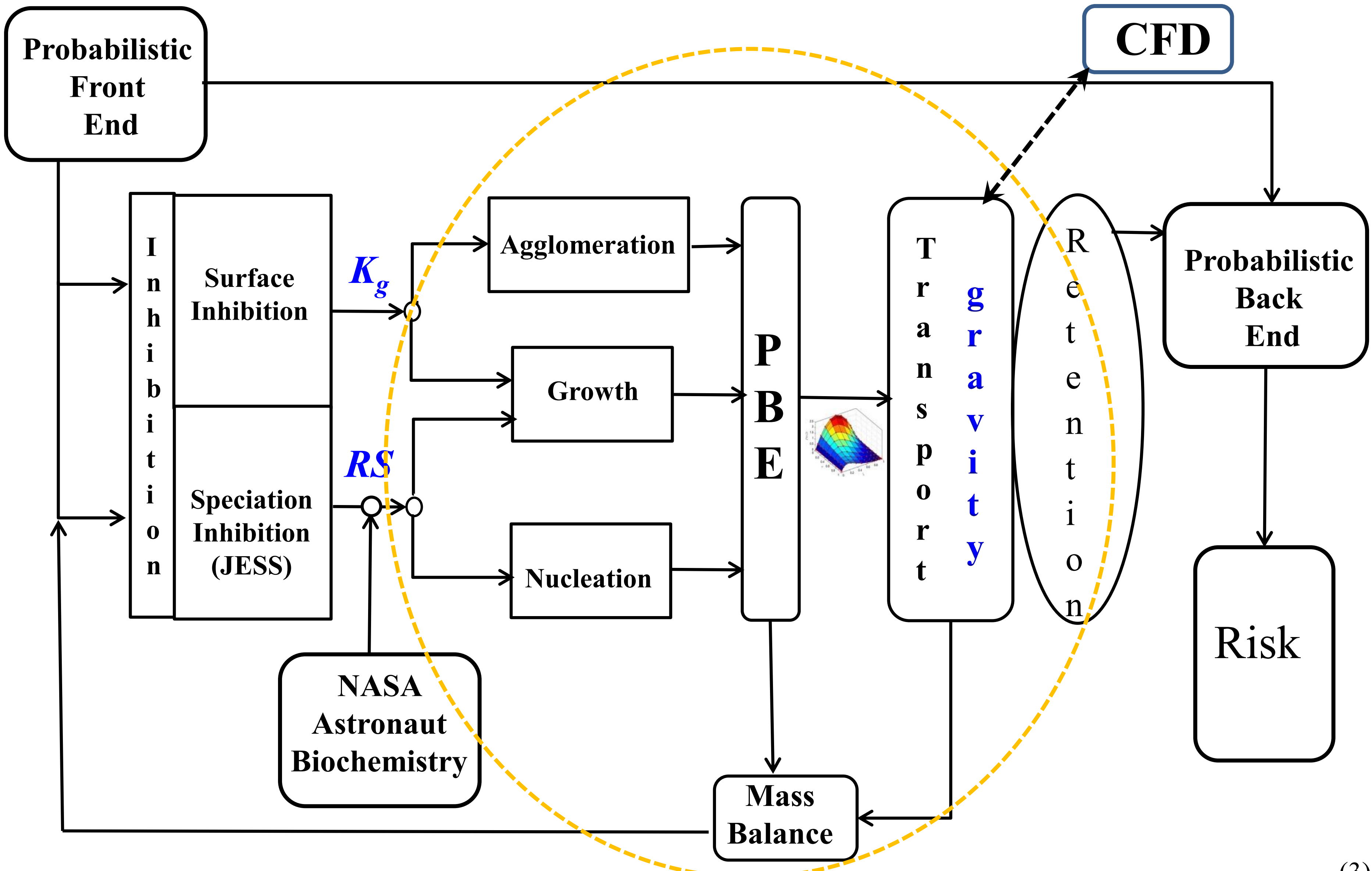




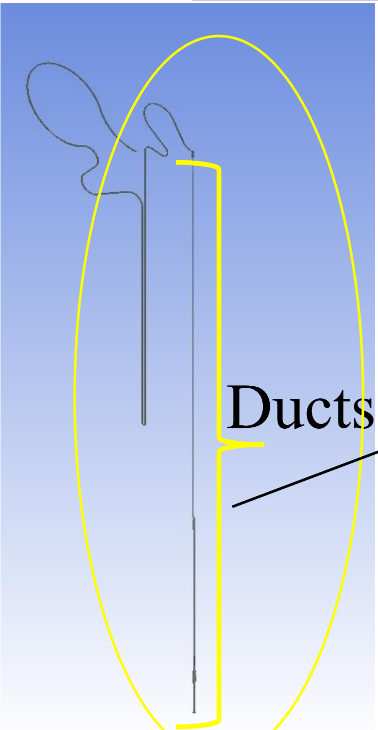
Renal Stone Formation Model (RSFM) was developed to address important NASA questions/needs in support of IMM:

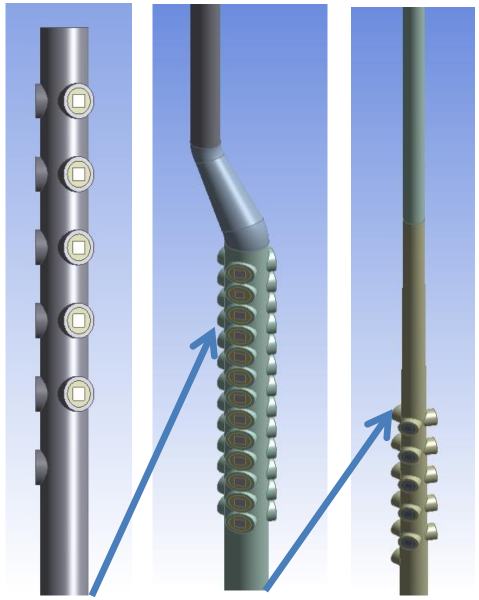
- Evaluate the risk of developing a critical renal stone incident during long duration microgravity missions based *on available astronaut biochemical data*
- Assess efficacy of countermeasures such as
  - Increase Hydration
  - Potassium Citrate & Magnesium
- Perform "*what if*" parametric studies to understand and assess risk of developing renal stone upon entry into a 1g or a remote partial gravitational field such as Mars or Moon where relevant astronaut biochemical data is unavailable

RSFM Model Development Flow Chart



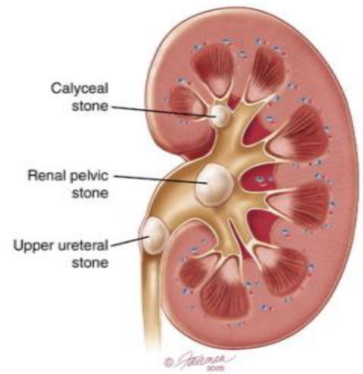
System & Multiphase CFD Models for Renal Stone Development & Transport in 1G and Microgravity

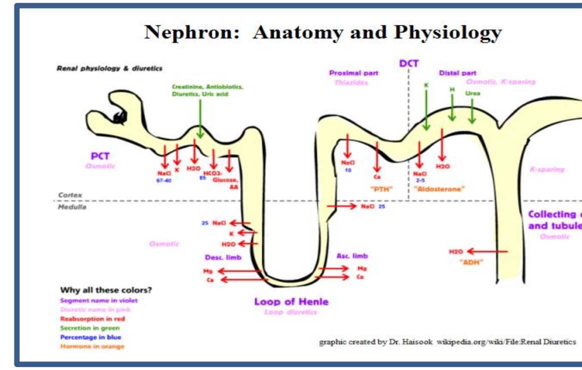




OMCD (200,000) IMCD (5,120) DoB (320)

Tubules(1,200,000)





Nephron Section	Length (mm)	Diameter (microns)	Net Volumetric Flow Rate (m^3/s)	Number of Flow Cells
Tubule	40	25	$8.06(10)^{-14}$	1,200,000
IMCD	16	33	$1.55(10)^{-13}$	200,000
OMCD	6	40	$5.40(10)^{-12}$	5,120
DoB	5	80	$2.72(10)^{-11}$	320

Major Simplifying Assumptions:

- Tubule section straight
- Microgravity
- Filteration/Secretion neglected
- Axisymmetry

Physio-Chemical Properties	Nominal Values
C_{Ca} (moles/L)	$3.27\ (10)^{-3}$
C_{Ox} (moles/L)	$2.41(10)^{-4}$
K_g (m/s)	$5.90\ (10)^{-10}$
K_b ($1/m^3$-s)	$5.90(10)^{7}$
b (m^3/s)	$2.78\ (10)^{-14}$
D_{nidus} (m)	$5\ (10)^{-7}$
a_{inlet}	10^{-8}
r_1 (kg/m^3)	1016
r_2 (kg/m^3)	2200
m_1 (Pa-s)	$8.3(10)^{-5}$
$D_{i\text{-}m}$ (m^2/s)	$1(10)^{-9}$

Renal Stone Population Balance Model: Nucleation, Growth & Agglomeration

Population Balance Equation:

MSMPRC

$$\frac{\partial n(v)}{\partial t} + \underbrace{\nabla \cdot [\vec{u}_2 n(v)]}_{\text{Growth}} + \underbrace{\nabla_v \cdot [G_v n(v)]}_{\text{Advection}} = \underbrace{\int_0^v \beta n(v - Dv')n(v')dv'}_{\text{Agglomeration-Birth}} - \underbrace{n(v)\int_0^\infty \beta n(v')dv'}_{\text{Agglomeration-Death}}$$

Nucleation BC:

$$n\,(D = 0) = n^o = {B^o}/{G_D}$$

Reaction/Growth Model :

$$G_D = K_D\,\{RS - 1\}^2$$

Nucleation Model :

$$B^o = K_B\{RS - 1\}^{2.88}$$

Relative Supersaturation:

$$RS = \left[\frac{C_{ca,\infty}^{Free}\, C_{Ox,\infty}^{Free}\, f_2^2}{K_{so}}\right]^{1/2}$$

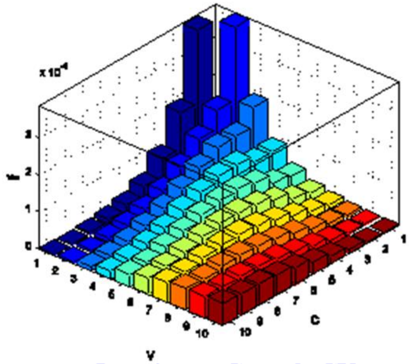
Important Problem Parameters

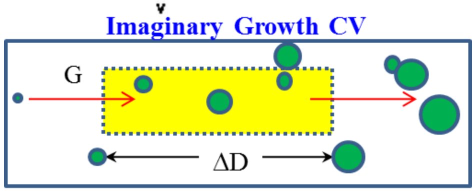
- K_B : Nucleation Rate Constant
- K_D : Growth Rate Constant
- β : Agglomeration Kernel
- RS: Relative Supersaturation

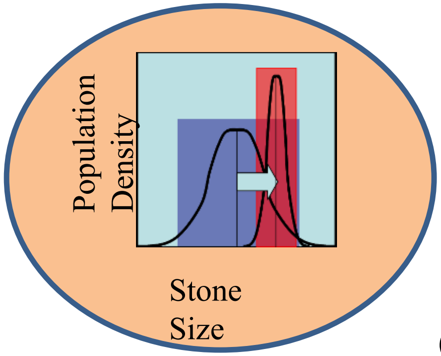
CaOx Volume fraction and Mass Transfer Uptake coupling to CFD

$$\alpha_2 = \int_0^{v_{max}} n(v)v\,dv$$

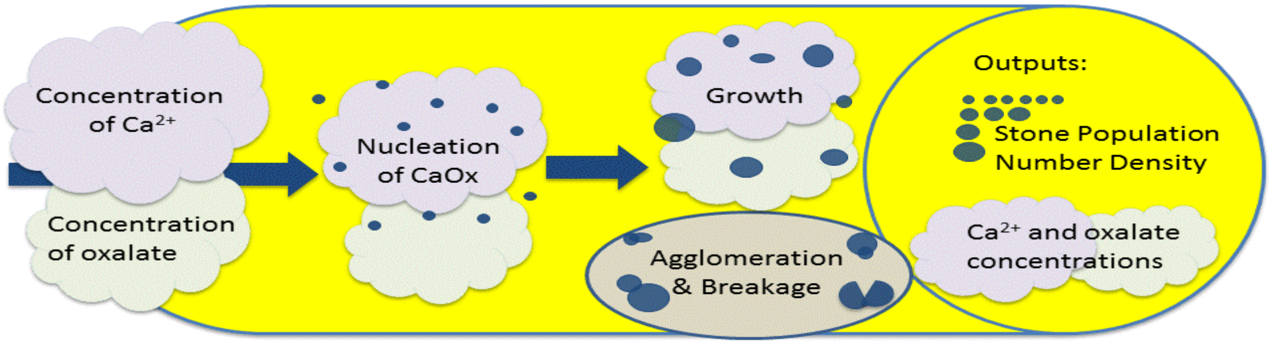
$$\dot{m}_{12} = \rho_1 \frac{\alpha_1}{\alpha_2} \int_0^\infty \frac{\pi}{2} G_v(v)n(v)dv$$







Coupling Stone PBE to Urinary Flow & Ca/Ox Transport in the Nephron using an Eulerian 2Phase CFD



Conservation of Mass:

$$\frac{\partial}{\partial t}(\propto_q \rho_q) + \nabla \cdot (\propto_q \rho_q \vec{u}_q) = \sum_{p=1}^{2} (\dot{m}_{pq} - \dot{m}_{qp})$$

Urine: q= 1

$CaOx$: q= 2

Momentum Equation:

$$\frac{\partial}{\partial t}(\propto_q \rho_q \vec{u}_q) + \nabla \cdot (\propto_q \rho_q \vec{u}_q \vec{u}_q) = -\alpha_q \nabla p + \nabla \cdot \bar{\bar{\tau}}_q + + \sum_{p=1}^{2} (\overrightarrow{R_{pq}} + \dot{m}_{pq} \vec{u}_{pq} - \dot{m}_{qp} \vec{u}_{qp})$$

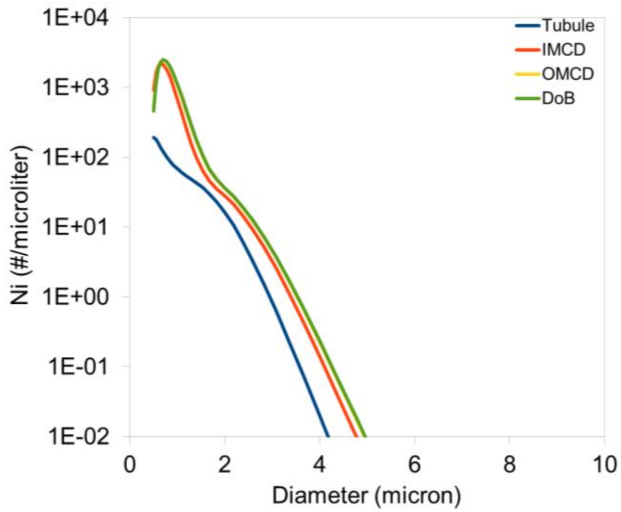
Conservation of Species:

$$\frac{\partial}{\partial t}(\propto_1 \rho_1 Y_j) + \nabla \cdot (\propto_1 \rho_1 \vec{u}_1 Y_j) = \nabla \cdot \alpha_1 \rho_1 D_{j,m} \nabla Y_j - \dot{m}_{12} Y_j$$

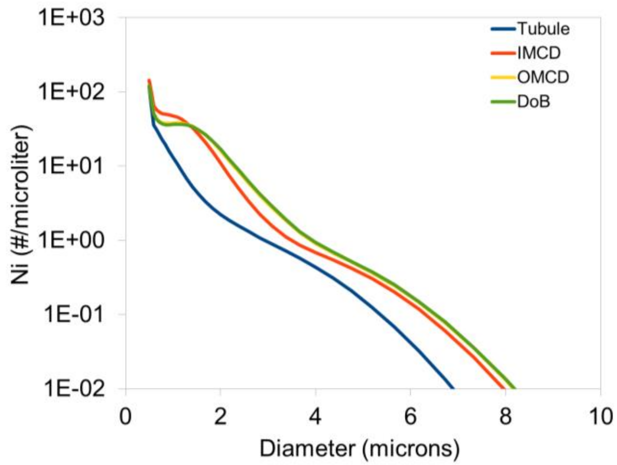
j = Ca, Ox

Comparison Between Normal and Astronaut Subjects in Space (Microgravity)

Normal Renal Biochemistry



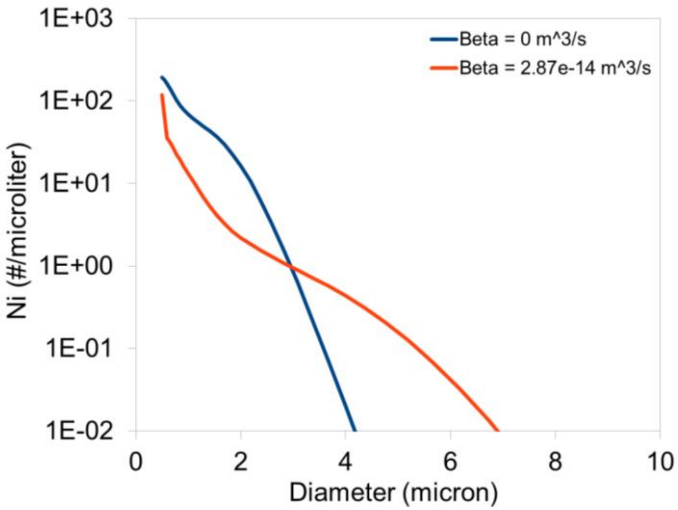
Astronaut Renal Biochemistry



- **1G normal:** risk-free range according to Litholink and UTSW 24 hr urine lab analysis designation
- **Microgravity astronaut:** 24hr urine sample -86 astronauts – day of landing- (Whitson et al, 1993)
- **Microgravity stone-former:** 24 hr urine sample –post long-duration flight (Whitson et al, 2009) – Worst case scenario constructed using the reported S.D. 🡐 *hypothetical*

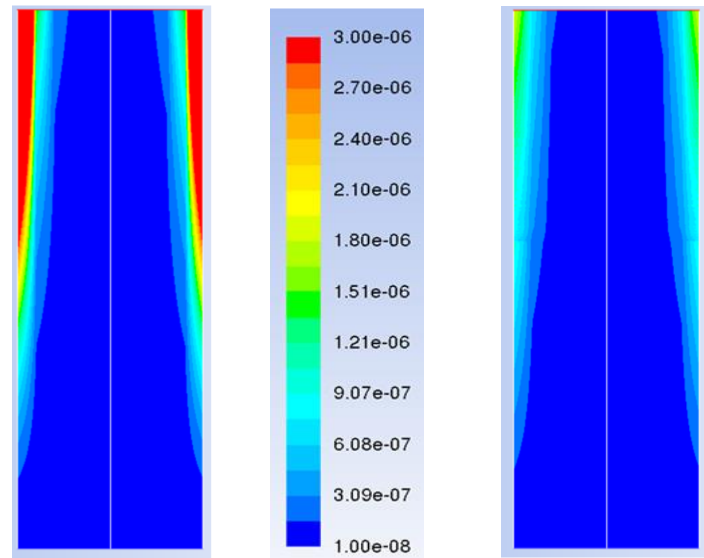
Effect of Agglomeration on Renal Calculi Size Distributions along the Nephron in Space

Tubule Section (40mm)

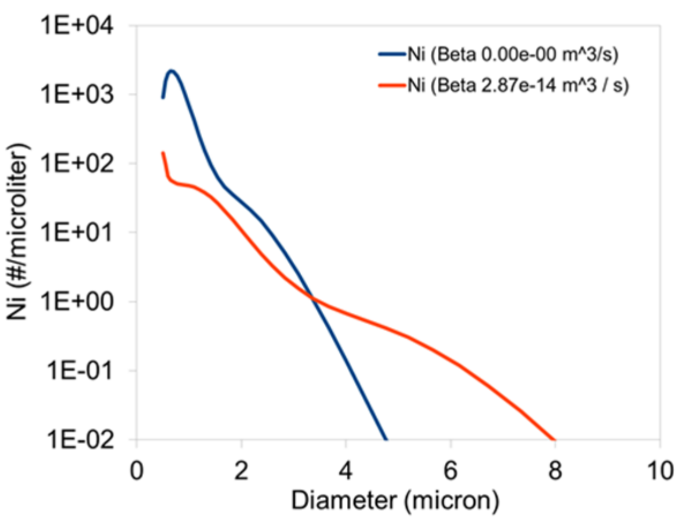


Non-Aggl.

Aggl.

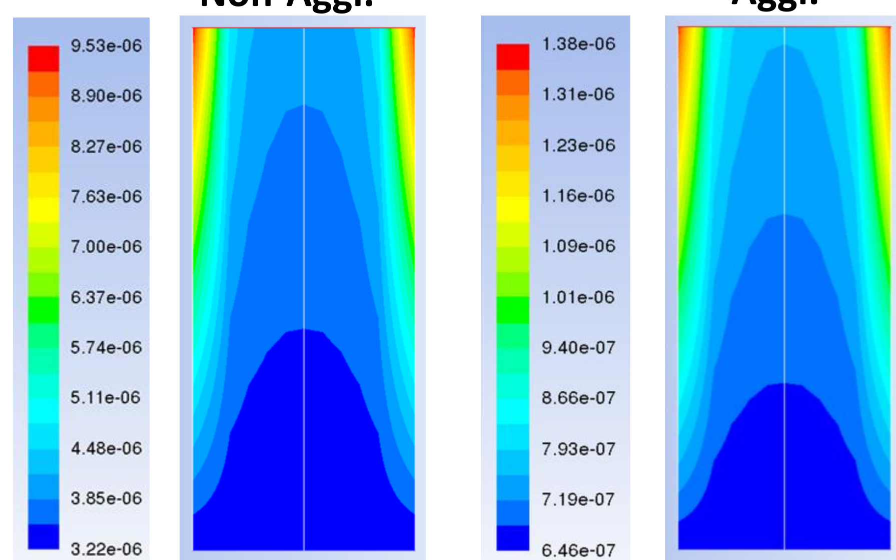


IMCD Section (16mm)



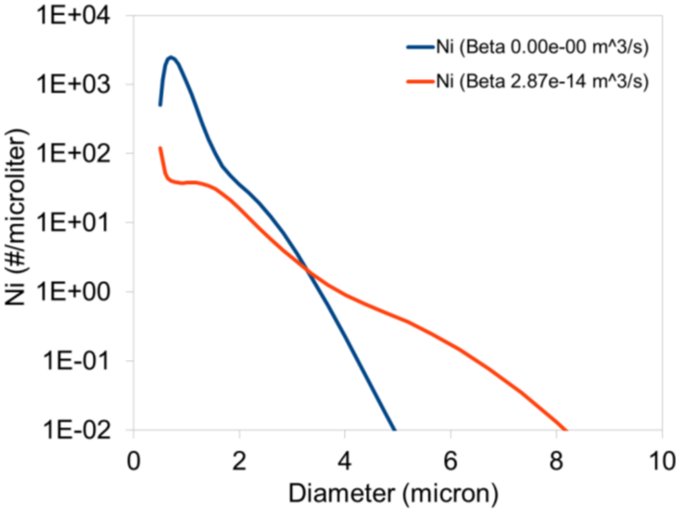
Non-Aggl.

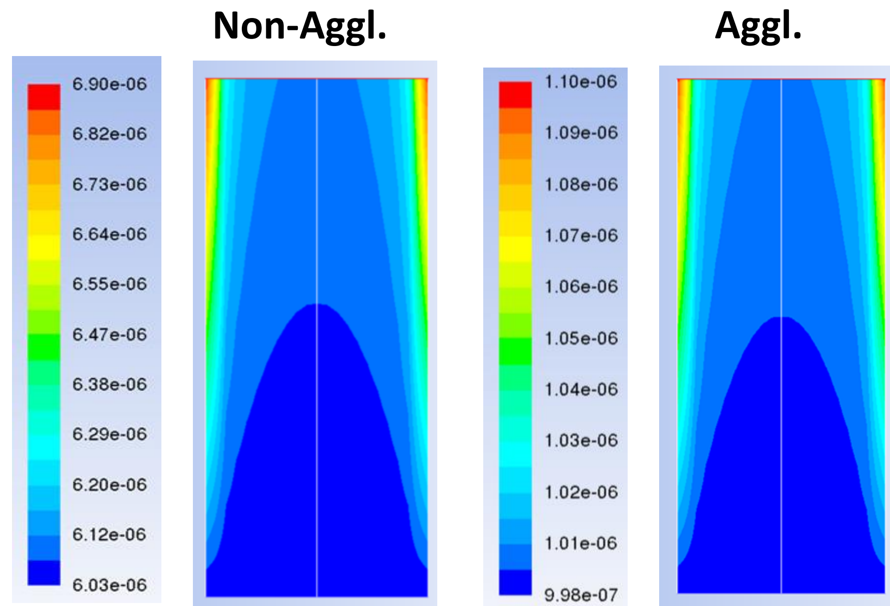
Aggl.



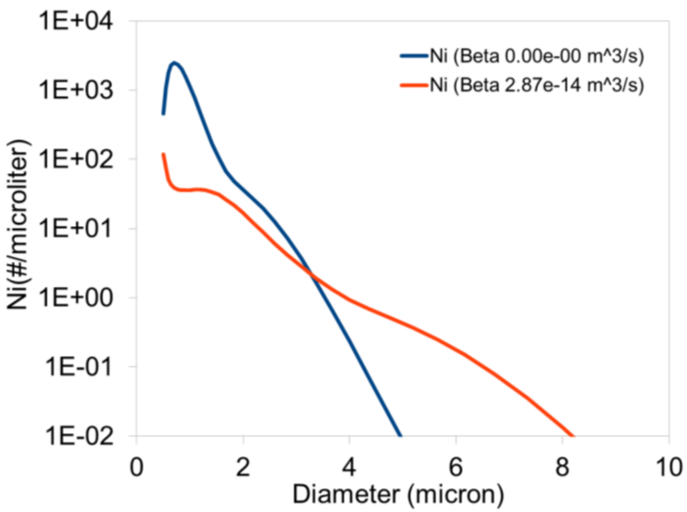
Effect of Agglomeration on Renal Calculi Size Distributions along the Nephron in Space

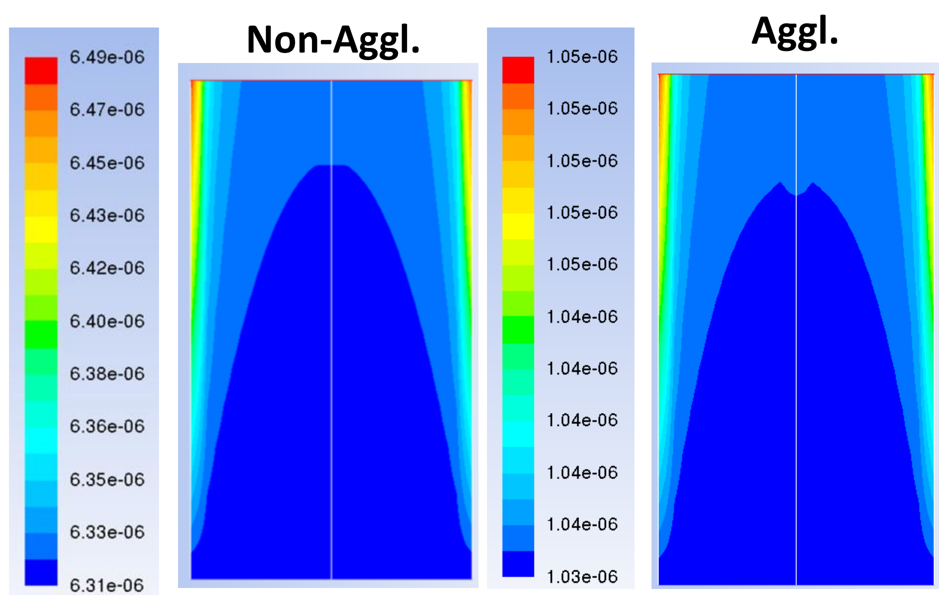
OMCD Section (6mm)





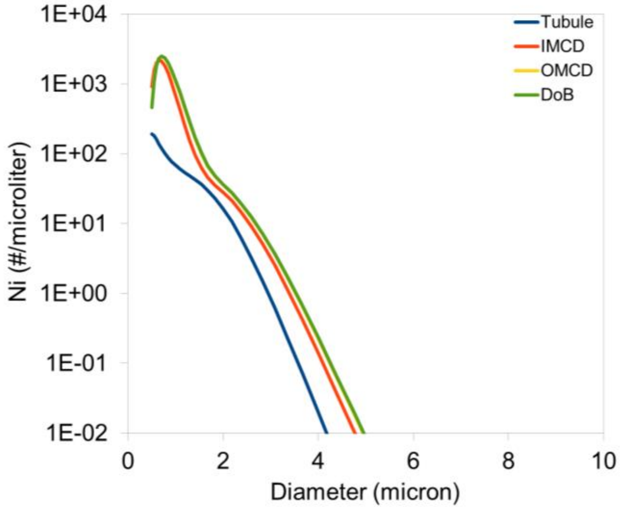
DoB Section (4mm)

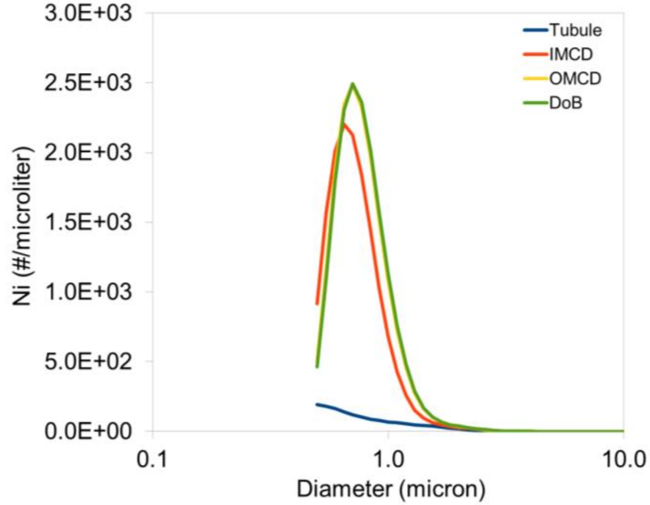




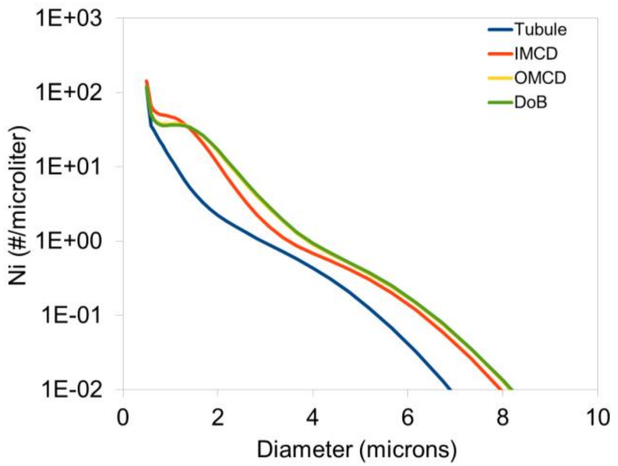
Effect of Agglomeration on Renal Calculi Size Distributions along the Nephron in Space

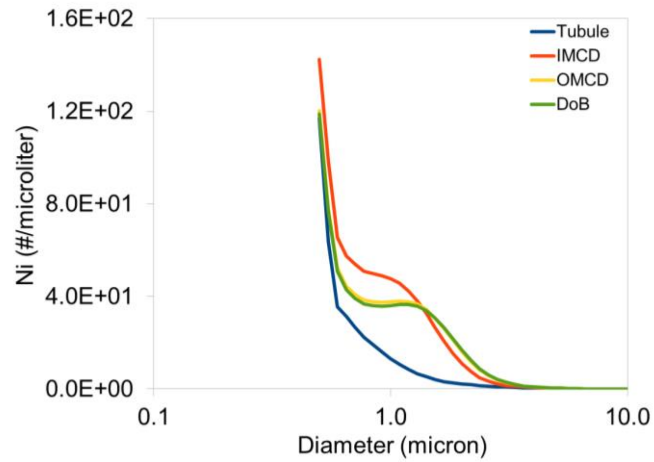
Non-Agglomeration





With Agglomeration

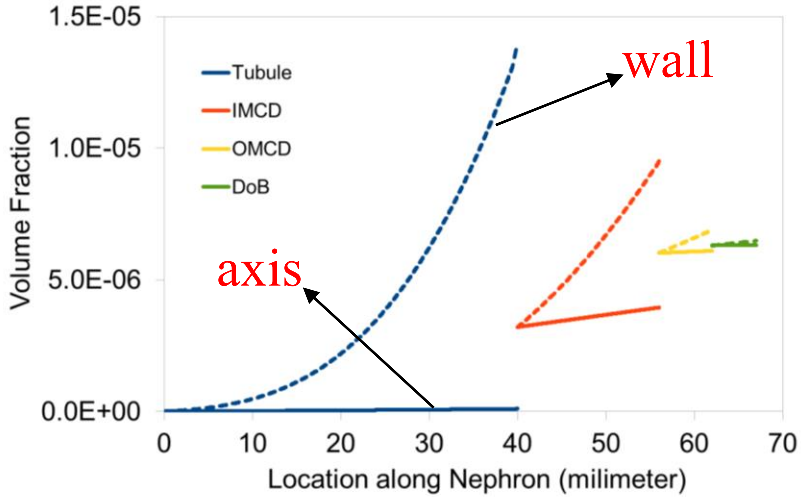




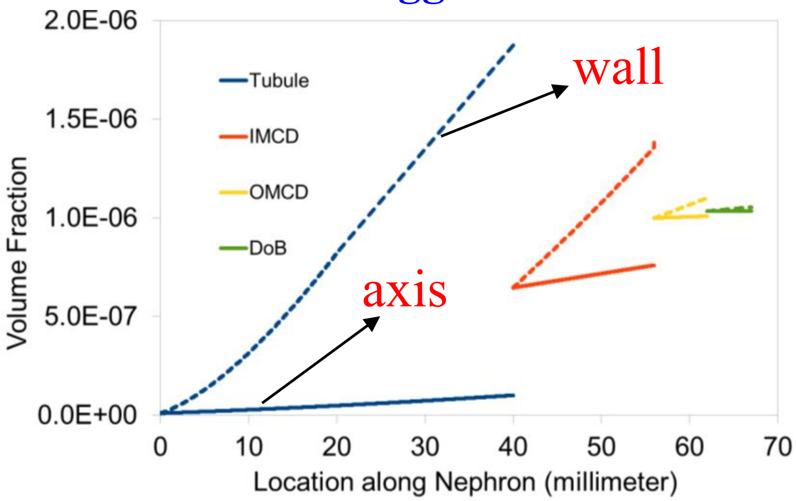
- Most of the CaOX size enhancement takes place in the Tubule and IMCD sections
- Agglomeration is a major mechanism for enlargement of renal calculi
- Growth-only results indicates a peak stone population at around 1 micron and limited sized single crystals.
- Agglomeration results indicate a peak population at nidus size but results in much larger size agglomerate formations

Effect of Agglomeration on Volume Fraction along the Nephron in Space

Non-Agglomeration

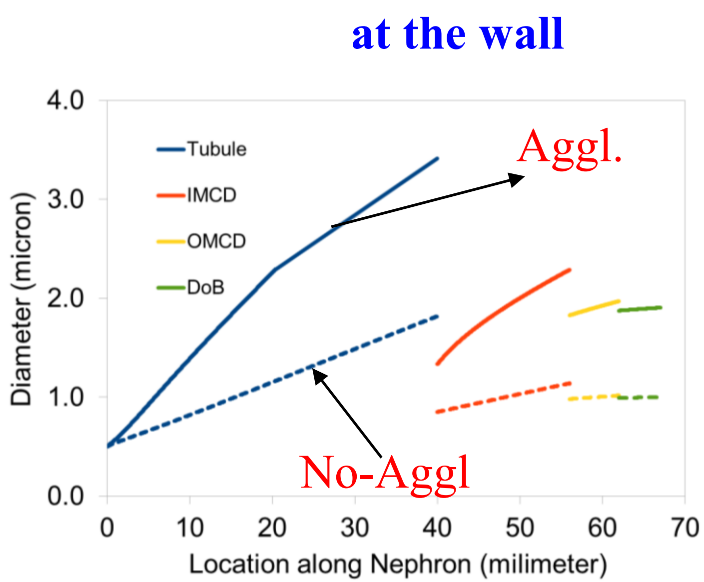


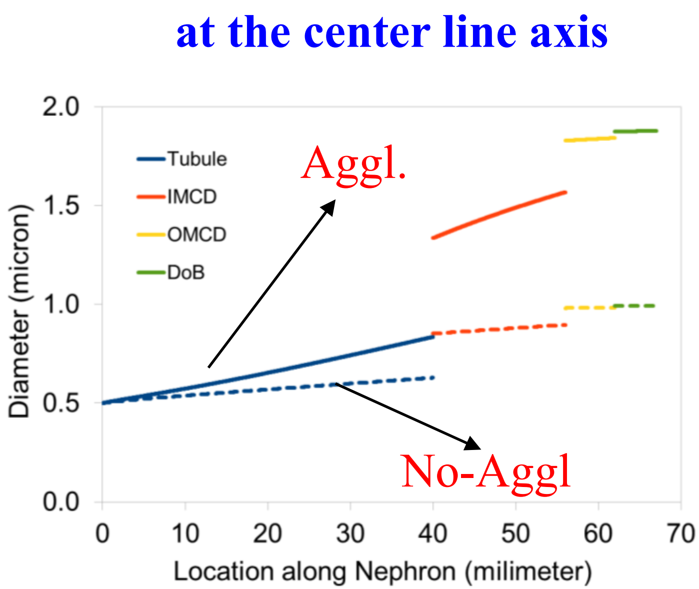
With Agglomeration



- Wall fraction considerably higher at the wall.
- Growth-only case results in higher volume fraction of stones in the nephron espcillay at the wall
- Quite non uniform volume fraction distributions in the tubule section
- Enhanced particle mixing (uniformizing effect) as urine travels down through the nephron as a result of mixing due to cascading geometry.
- Mixed Suspension Mixed Product Removal (MSMPR) assumption only valid in the OMCD and DoB sections

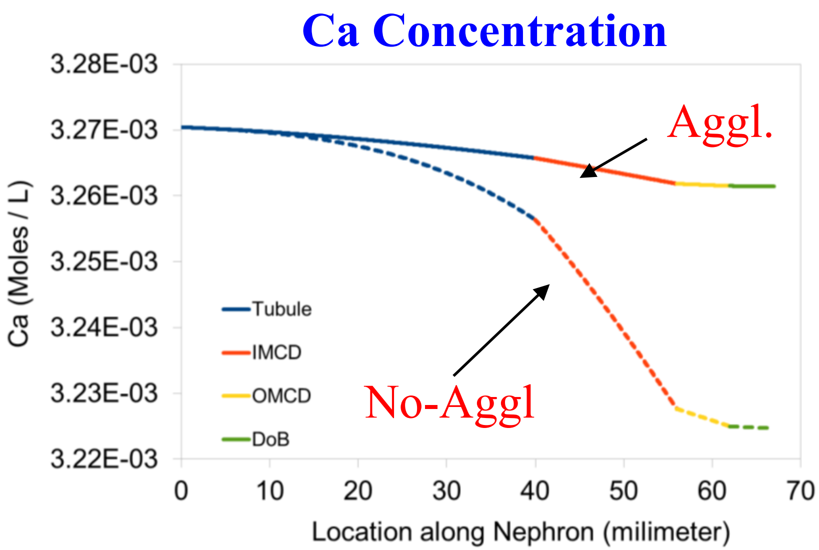
Effect of Agglomeration on Mean CaOx Particle Diameter along the Nephron in Space

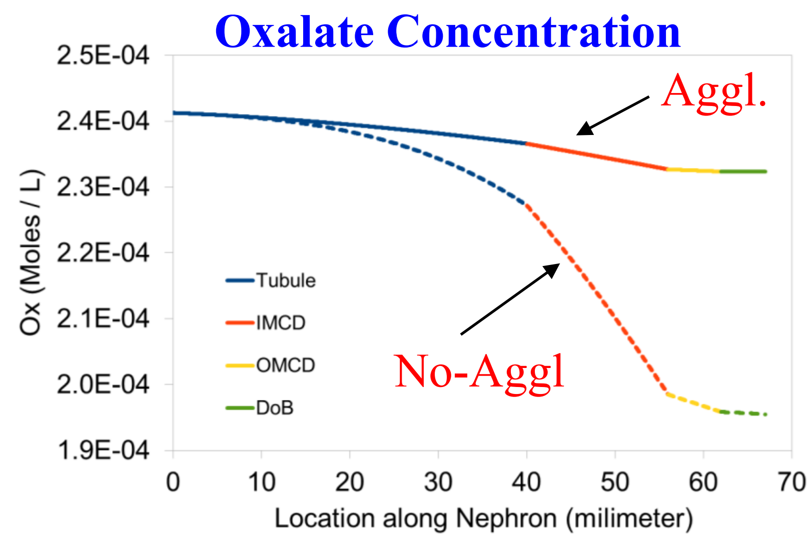




- Largest particles formed at the wall.
- Although agglomeration decreases the average stone volume fraction in the nephron it still produces the largest particles as compared to the growth-only situation especially at the nephron wall.
- Cascading effect decreases the mean calculi diameter as urine travels along the nephron.

Effect of Agglomeration on Ca and Ox Distributions along the Nephron in Space





- Depletion of Ca and Ox occurs all along the nephron but is largest in the Tubule and IMCD sections
- Depletion effect is more pronounced in the absence of agglomeration where most of the size enhancement occurs through nucleation and growth.
- Uptake of Ca and Ox are decreased by agglomeration since most of the size enhancement occurs through adhesion of particles together thus promoting enlargement while minimizing the effective surface area for interphase mass transfer.

Closure & Future Path

- Numerical prediction based on astronaut urinary data indicate that due to renal biochemical changes in Space, an astronaut is subject to increased but still considerably subcritical risk.
- Agglomeration was found to be a very strong mechanism for CaOx aggregate size enhancement. Reliable data of the agglomeration rate constant for CaOx in urine is much needed.
- Most of the renal calculi size enhancement occurs in the Tubule and IMCD sections.
- There is large cross-sectional variation of stone volume fraction in the Tubule and IMCD sections with layering of the largest particles near the nephron wall. Thus the concept of a MSMPR reactor might be only valid for the OMCD and DoB segments.
- Thus, the Tubule and IMCD sections can be regarded as the crystallizer sections and the OMCD and DoB as the particulate uniformizer segments of the nephron.
- Depletion effect is highest under non-agglomeration conditions especially in the Tubule and IMCD sections.
- Important factors to be considered in futures studies:
  - Effect of gravity
  - Effect of 3D convoluted Tubule geometry
  - Effect of variable Ca and OX concentrations due to reabsorption/secretion nephron processes.

Extra slides