Mathematical modeling of biodegradation of metallic biomaterials using reaction-diffusion-convection equations and level set method

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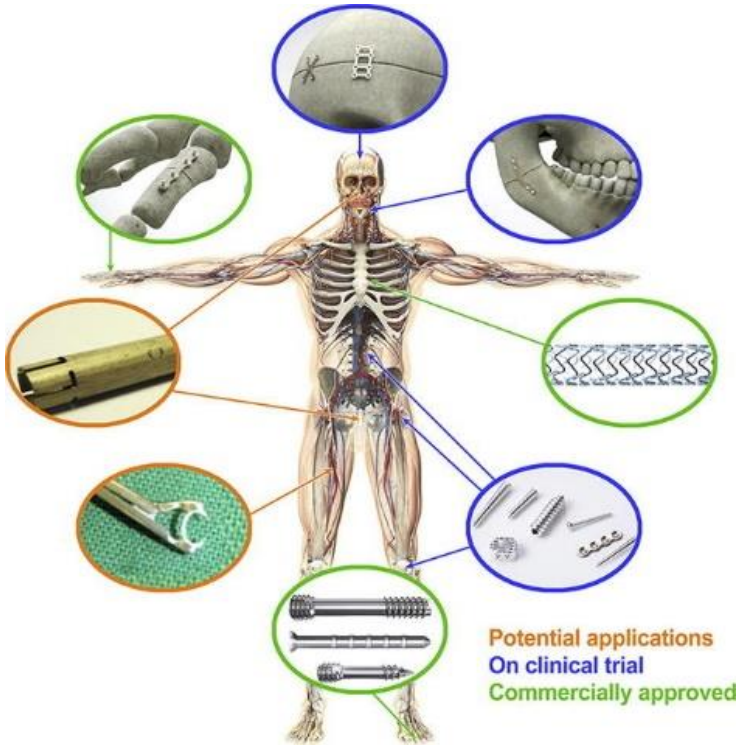
Biodegradable Metals

- Mg, Zn, and Fe
- Gradually disappear/absorbed and replaced by new tissue/bone
- Great mechanical/biological properties
- The controlled release is an issue for different types of implants
- The degradation behavior should be tuned/optimized for various applications

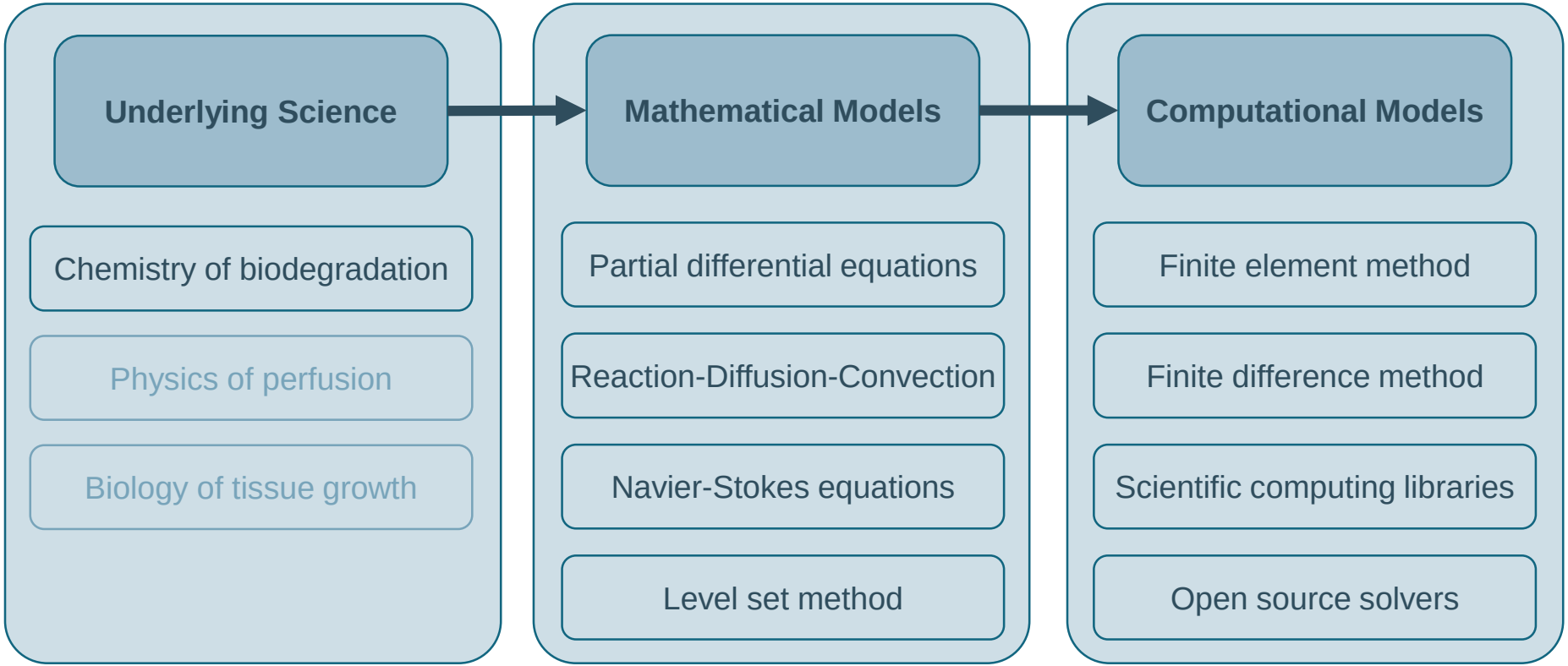


(Han et al., Mater. Today, 23, 2019)

Problem Definition

- Challenge:
  - Tuning the biodegradation to the regeneration of the new tissue/bone
- Can be solved by:
  - Mathematical modeling of biodegradation
  - Coupling biodegradation models with tissue growth models
  - Considering environmental effects

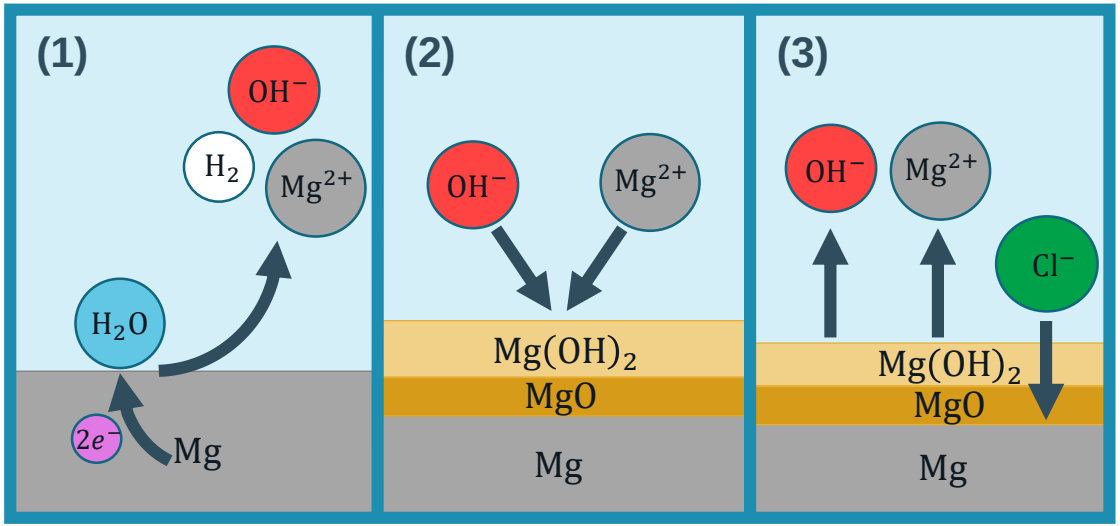
Modeling Workflow



Chemistry of Biodegradation

The model captures:

1. The chemistry of dissolution of metallic implant
2. Formation of a protective film
3. Effect of ions in the medium
4. Change of pH



Mathematical Representation

Chemical reactions

$$Mg + 2H_2O \xrightarrow{k_1} Mg^{2+} + H_2 + 2OH^- \xrightarrow{k_1} Mg(OH)_2 + H_2$$

$$Mg(OH)_2 + 2Cl^- \xrightarrow{k_2} Mg^{2+} + 2Cl^- + 2OH^-$$

State variables

$$C_{Mg} = C_{Mg}(\mathbf{x}, t) \quad C_{Film} = C_{Film}(\mathbf{x}, t)$$
$$C_{Cl} = C_{Cl}(\mathbf{x}, t) \quad C_{OH} = C_{OH}(\mathbf{x}, t) \quad \mathbf{x} \in \Omega \subset \mathbb{R}^3$$

Derived Partial Differential Equations

$$\frac{\partial C_{Mg}}{\partial t} = \nabla . \left(D^e_{Mg} \nabla C_{Mg}\right) - k_1 C_{Mg} \left(1 - \beta \frac{C_{Film}}{[Film]_{max}}\right) + k_2 C_{Film} {C_{Cl}}^2$$

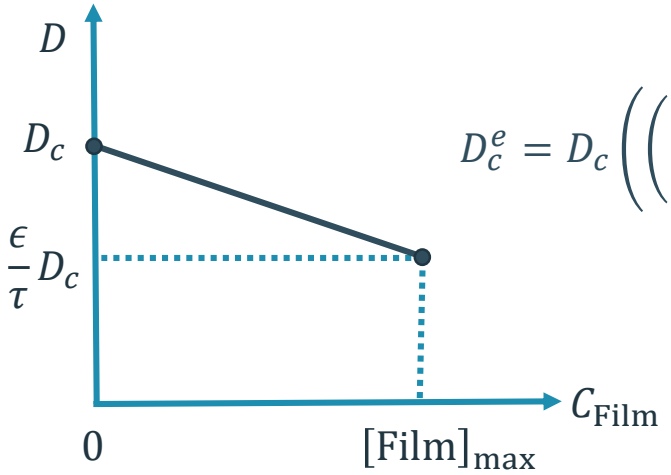
$$\frac{\partial C_{Film}}{\partial t} = k_1 C_{Mg} \left(1 - \beta \frac{C_{Film}}{[Film]_{max}}\right) - k_2 C_{Film} {C_{Cl}}^2$$

$$\frac{\partial C_{Cl}}{\partial t} = \nabla . \left(D^e_{Cl} \nabla C_{Cl}\right)$$

$$\frac{\partial C_{OH}}{\partial t} = \nabla . \left(D^e_{OH} \nabla C_{OH}\right) + k_2 C_{Film} {C_{Cl}}^2$$

Calculating Effective Diffusion Coefficients

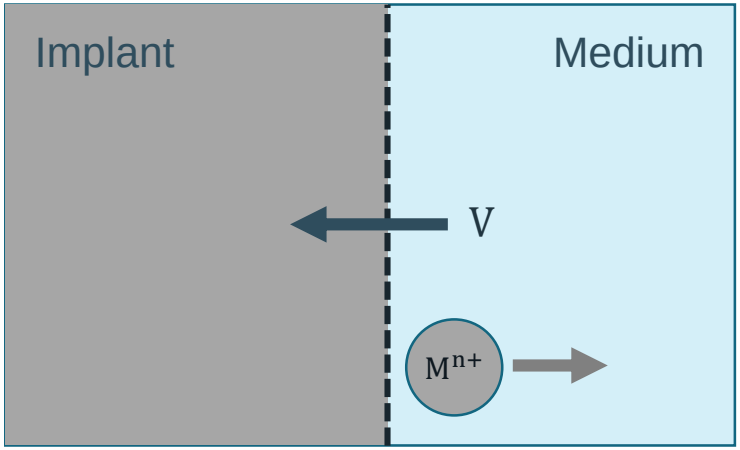
- Formed protective film is a porous material
- Effective diffusion coefficients can be calculated by interpolation



$$D_c^e = D_c \left(\left(1 - \frac{C_{\text{Film}}}{[\text{Film}]_{\max}} \right) + \frac{C_{\text{Film}}}{[\text{Film}]_{\max}} \frac{\epsilon}{\tau} \right)$$

Capturing the Moving Interface

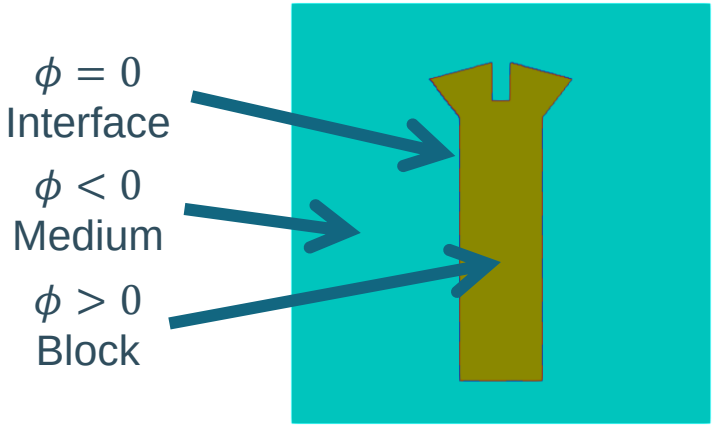
- Identifying interface is crucial in this research
- Mathematical representation of the interface

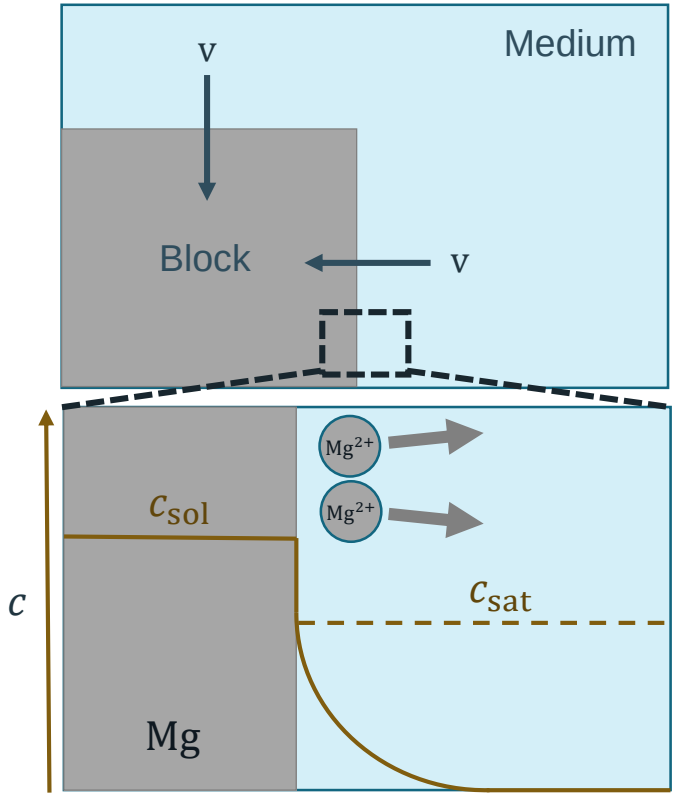


Capturing the Biodegradation Interface

- Implicit moving interface tracking
- Level set method

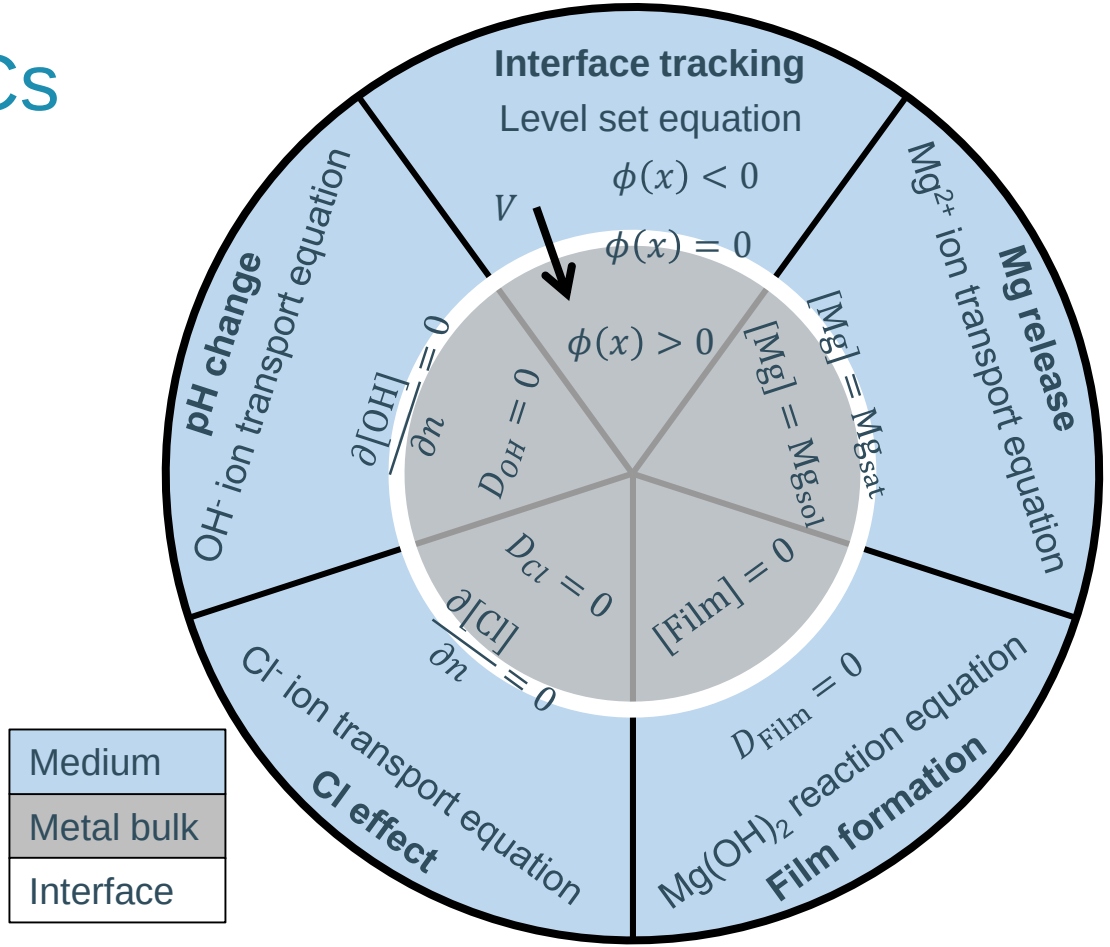
PDE to solve: $$\frac{\partial \phi}{\partial t} - \frac{D^e_{\mathrm{Mg}} \nabla_n C_{\mathrm{Mg}}}{[\mathrm{Mg}]_{\mathrm{sol}} - [\mathrm{Mg}]_{\mathrm{sat}}} |\nabla \phi| = 0$$





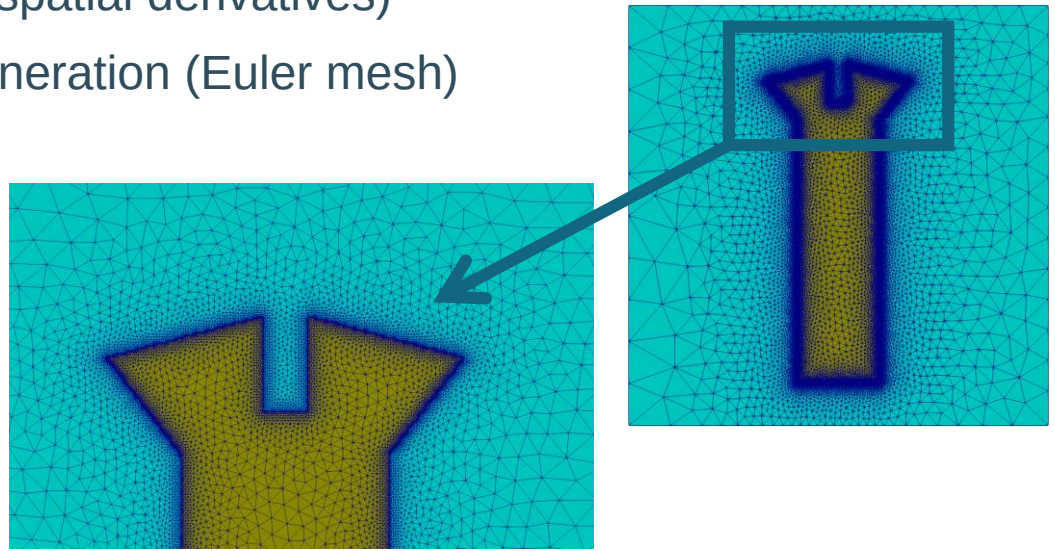
Constraints and BCs

- Interface tracking
- Magnesium ion transport
- Protective film formation
- Chloride ion transport
- Hydroxide ion transport



Constructing Computational Model

- Discretizing PDE equations, numerical computation
  - Finite difference method (temporal derivatives)
  - Finite element method (spatial derivatives)
- Adaptively refined mesh generation (Euler mesh)



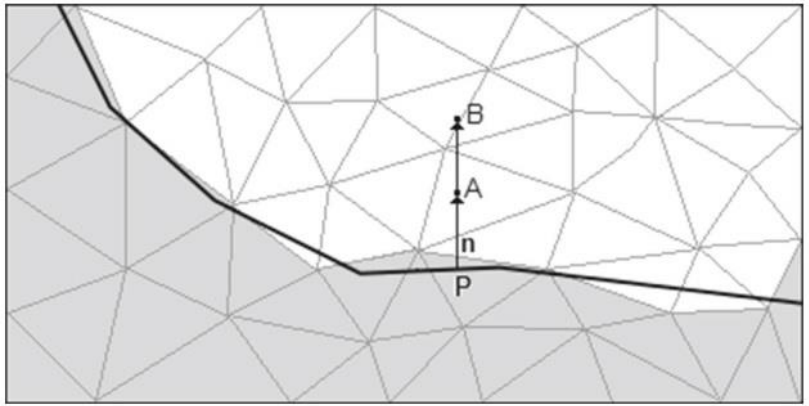
Implementing Computational Model

- Mesh generation (SALOME, Mmg), #Element ~ 10,000,000
- Weak form implementation (FreeFEM), #DoF ~ 2,000,000
- Parallelization is essential
  - High-performance domain decomposition (HPDDM)
  - High-performance preconditioners and solvers (PETSc)
- Paralleled IO postprocessing (ParaView)

Level Set Implementation

- Penalization for interface BCs
- Problem of concentration oscillation
- Computing $\nabla_n C_{\mathrm{Mg}}$ correctly
- Problem of re-distancing the distance function ϕ

$$\nabla_n C = \frac{C(\mathbf{x} + h.n) - C(\mathbf{x} + 2h.n)}{h},$$
$$\mathbf{x} \in \Omega \subset \mathbb{R}^3$$



(Bajger et al., Biomech. Model., 2017)

Computing Mass Loss - Degradation Rate

- Measuring mass loss:
  - Direct weight reduction
  - Side products evolution (hydrogen)
- Using level set output for calculating mass loss

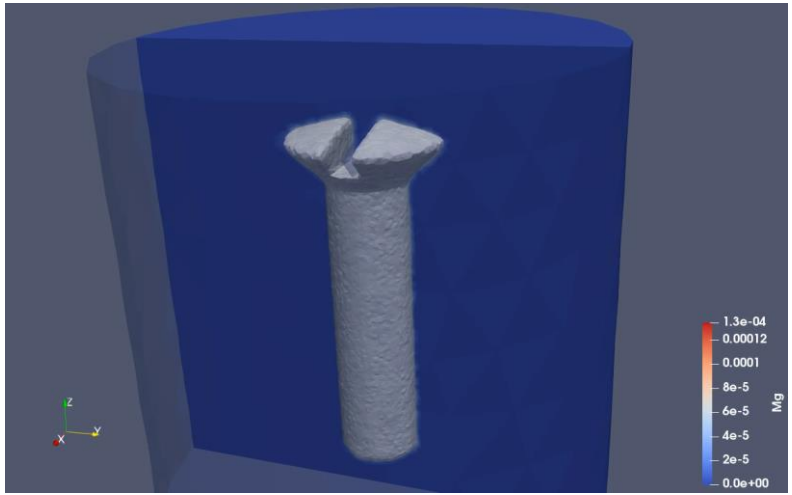
$$\mathrm{Mg}_{\mathrm{lost}} = \int_{\Omega_+(t)} [\mathrm{Mg}]_{\mathrm{sol}} \mathrm{d}V - \int_{\Omega_+(0)} [\mathrm{Mg}]_{\mathrm{sol}} \mathrm{d}V \qquad \Omega_+(t) = \{\mathbf{x}: \phi(\mathbf{x}, t) \geq 0\}$$

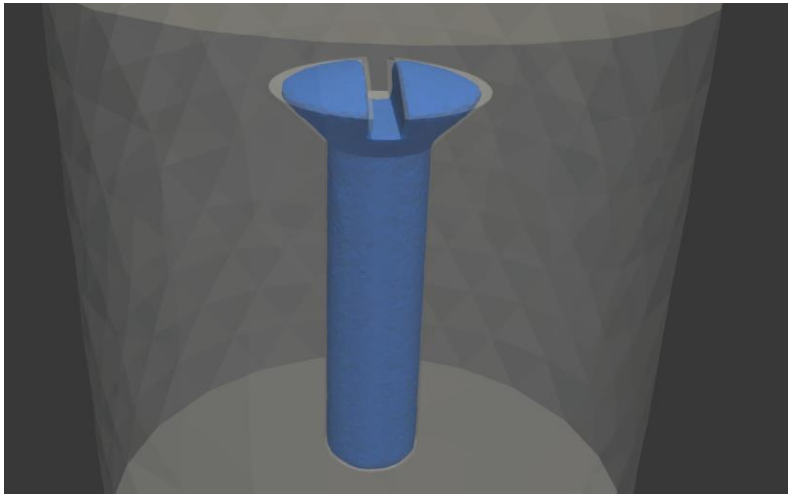
$$H_f = \frac{\mathrm{Mg}_{\mathrm{lost}}}{\mathrm{Mg}_{\mathrm{mol}}} \frac{RT}{P}$$

Verification of the Developed Model

Verifying the correct behavior of:

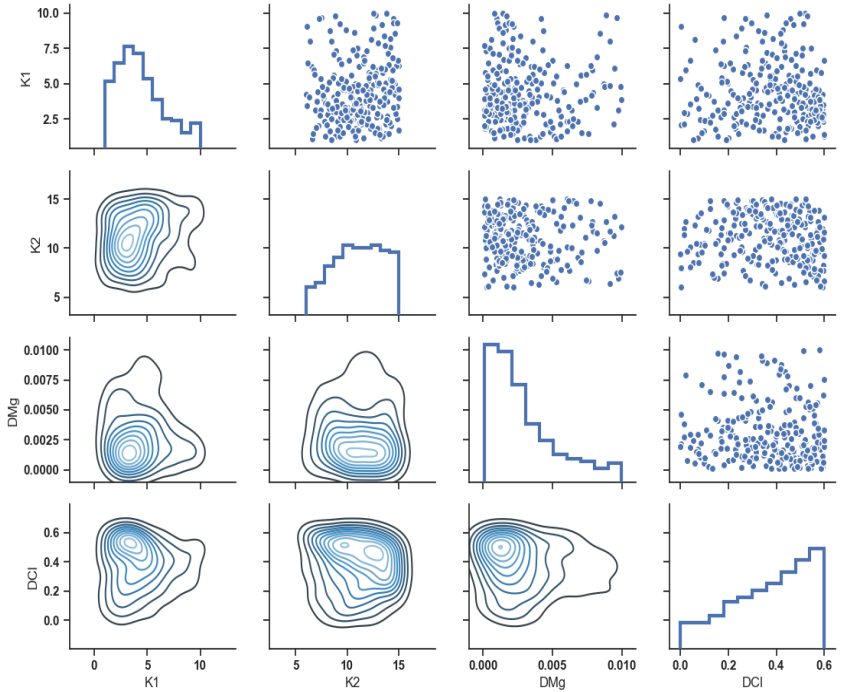
- Mass transfer and ion release
- Level set surface tracking





Model Parameters Estimation

- Sensitivity analysis to get the important parameters in different diffusion regimes
- Using a Bayesian optimization algorithm for estimating the effective parameters
- Each optimization iteration takes several hours to complete (another reason for the necessity of parallelization)



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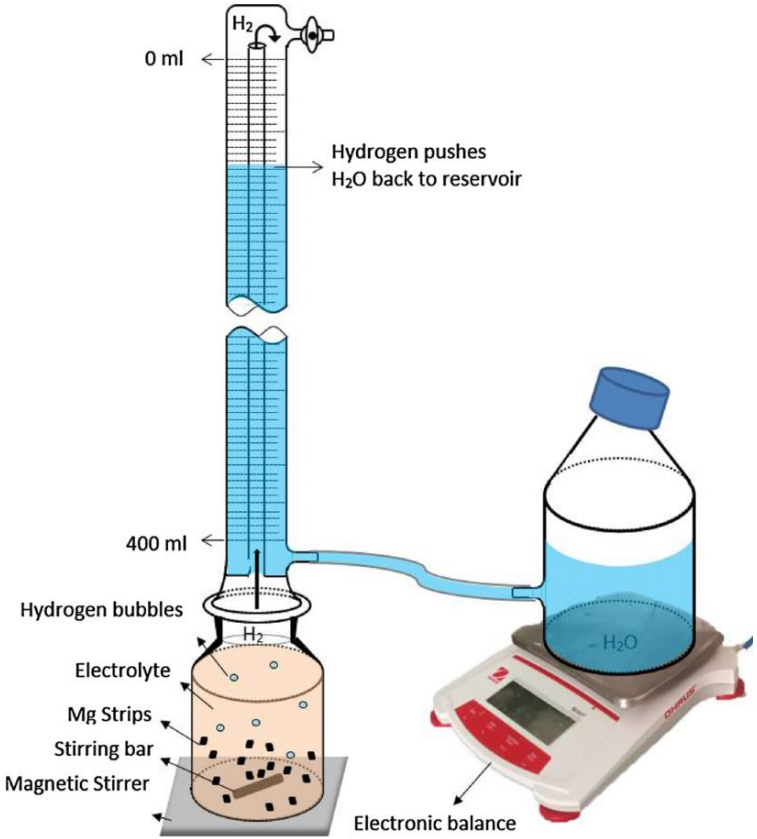
Model Validation

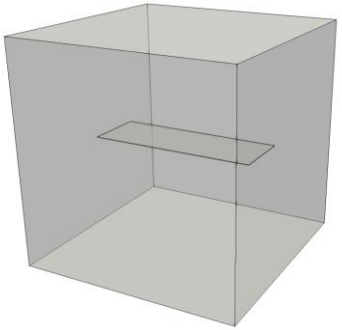
- Immersion tests in simulated body fluid (SBF) and saline (NaCl) solutions
- Measuring mass loss indirectly via measuring the formed hydrogen
- The global pH is monitored and used to validate the model

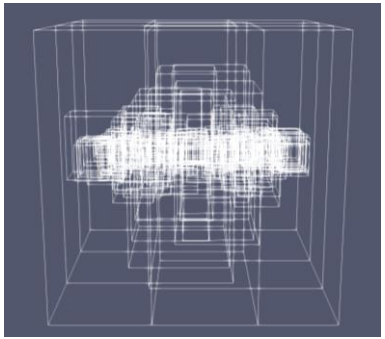


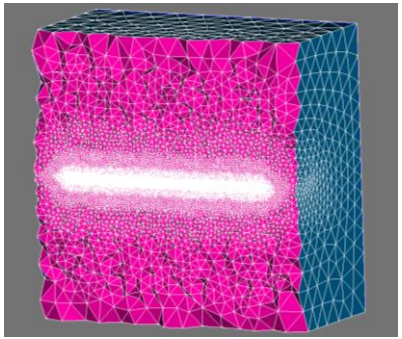
(Mei et al., Corrosion Science, 2019)

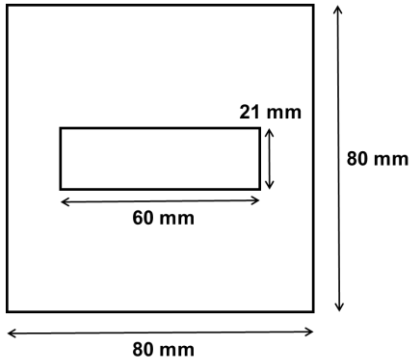
Simulation Setup

- A narrow cuboid of Mg in SBF/Saline solutions
- Simulating 21 hours of degradation
- ~18,000,000 elements (DoF of ~3,000,000)
- Parallelized using 170 computing nodes

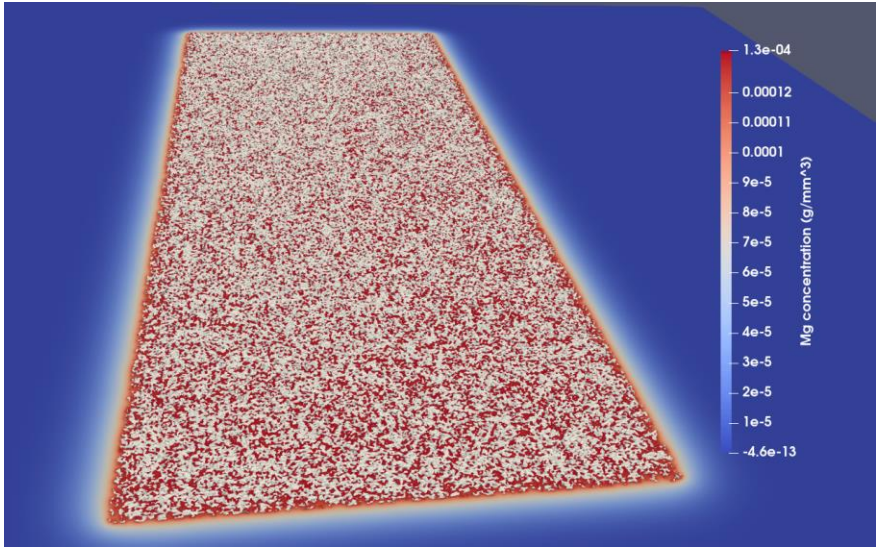




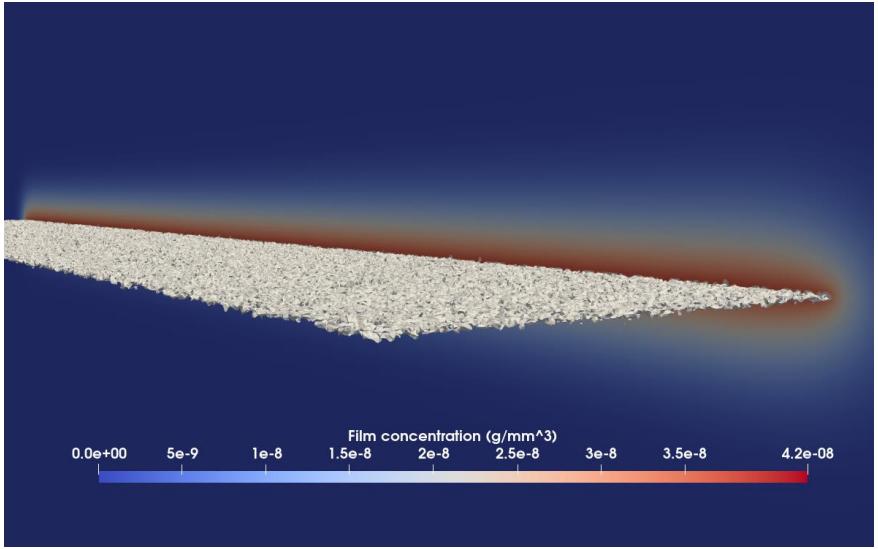




Simulation Results - Degradation

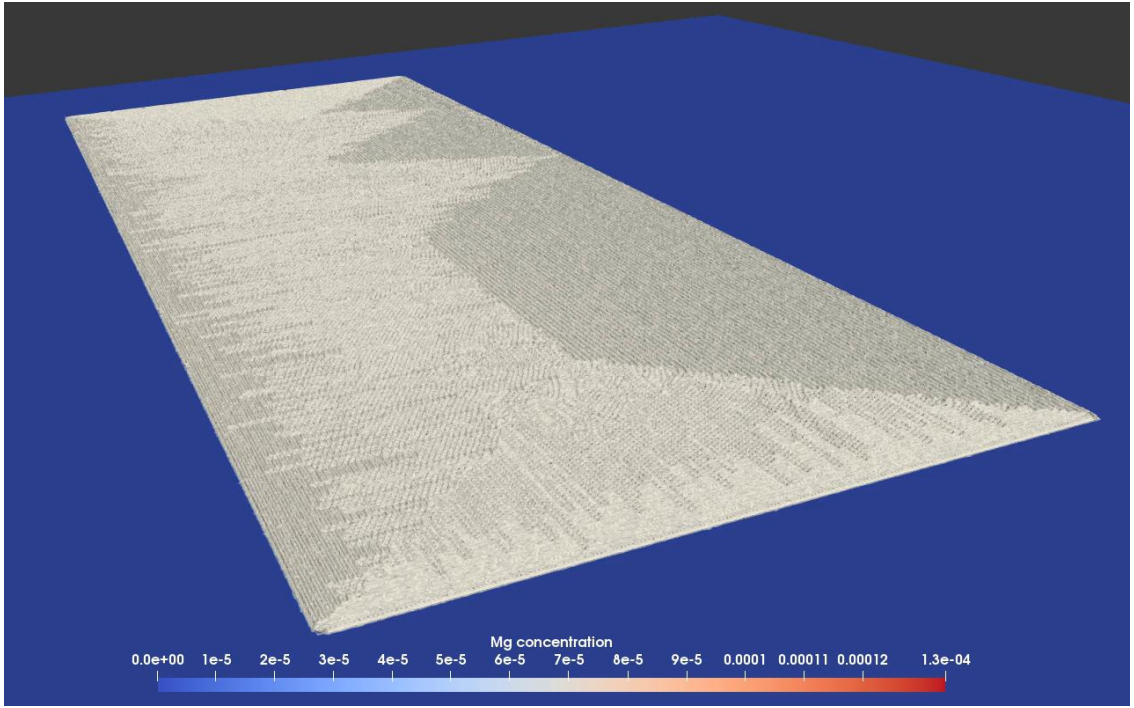


Release of Mg ions

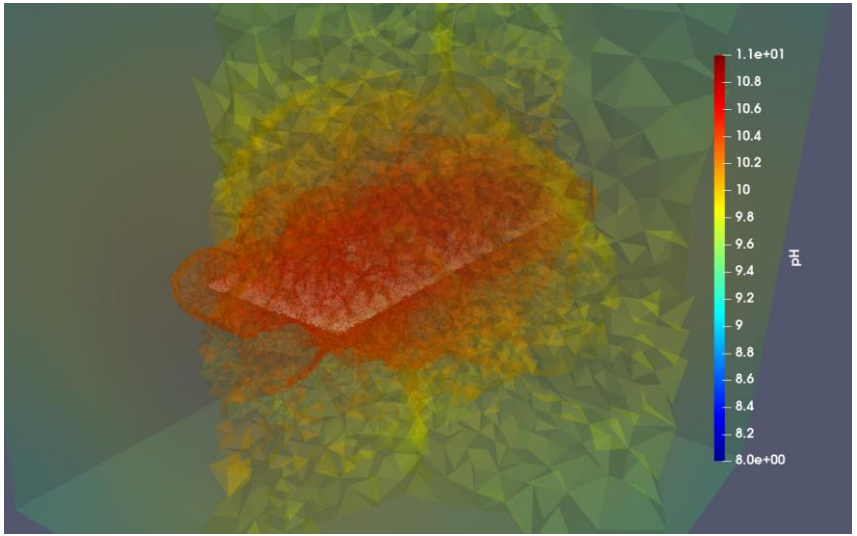


Formation of the protective film

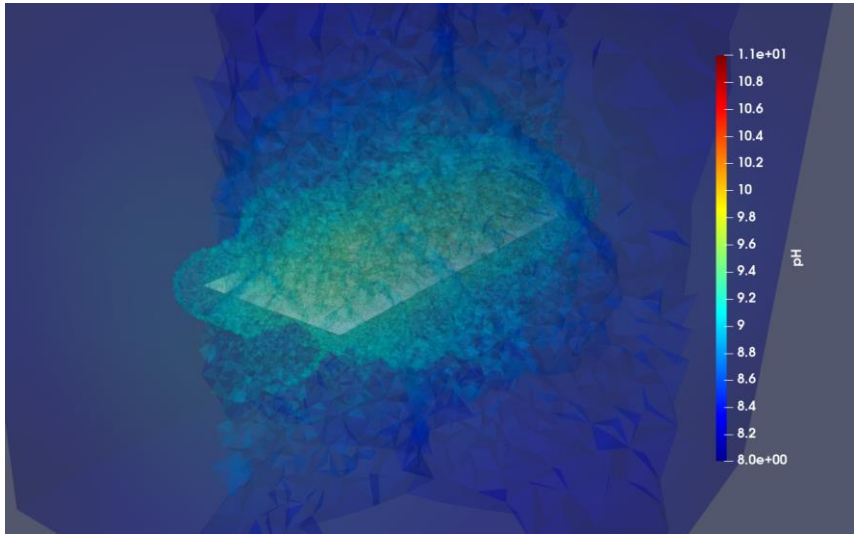
Simulation Results - Degradation



Simulation Results - pH Change

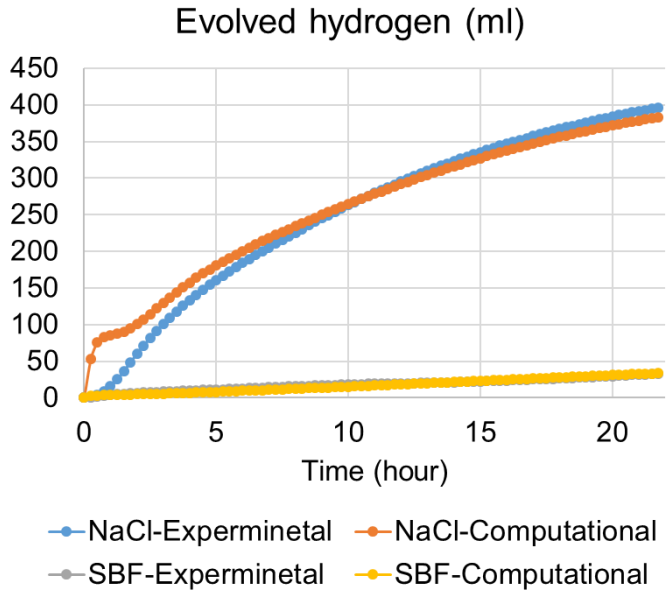


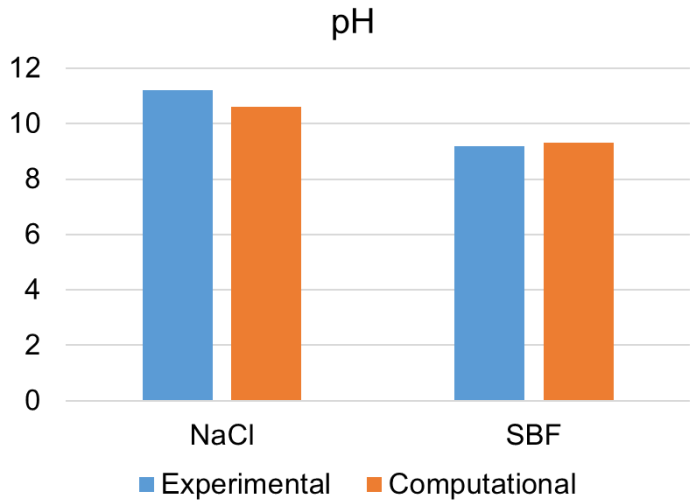
High diffusion
(NaCl solution – high diffusion rate)



Low diffusion
(SBF solution – low diffusion rate)

Quantitative Results

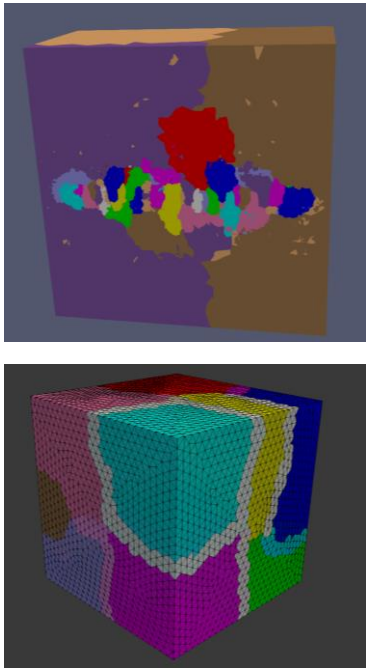




A Bit of the Parallelization Details

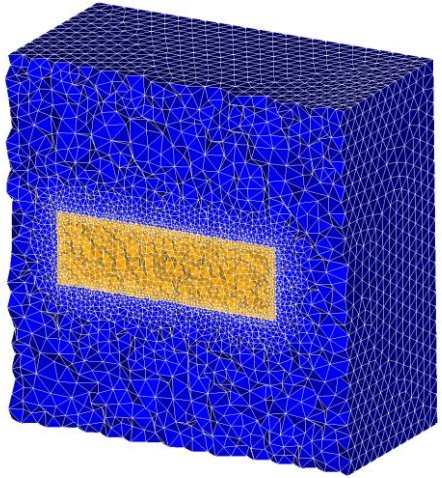
- Distributing the mesh among available resources
  - High-performance mesh decomposition
  - Overlapping Schwarz method
- Solving the linear system of equations
  - HYPRE preconditioner
  - GMRES iterative solver

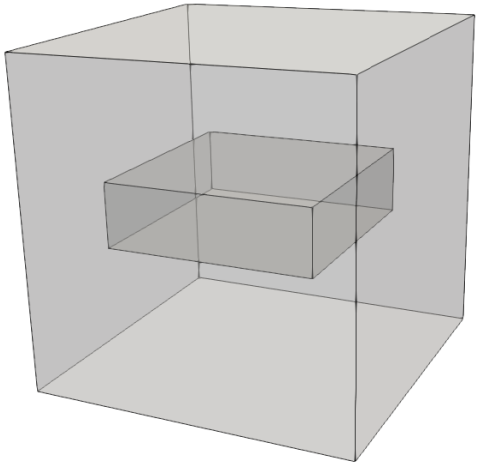
$$M^{-1}Ax = M^{-1}b$$



Performance Analysis

- Similar setup with a thicker block
- Only 3 PDEs are solved (Mg, film formation, and level set)
- DOF for each PDE ~ 144,000
- Elements ~ 831,000

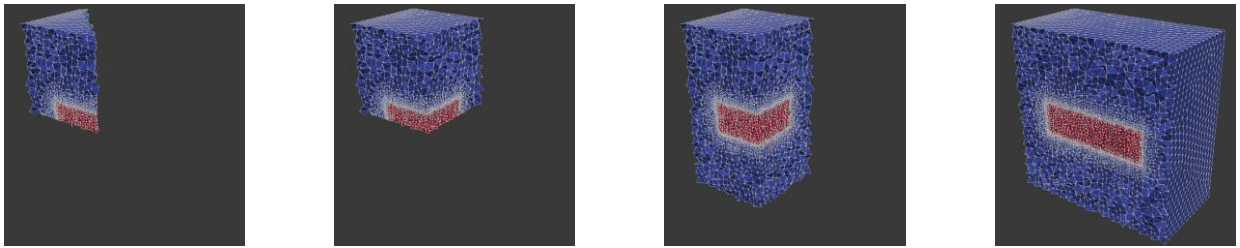




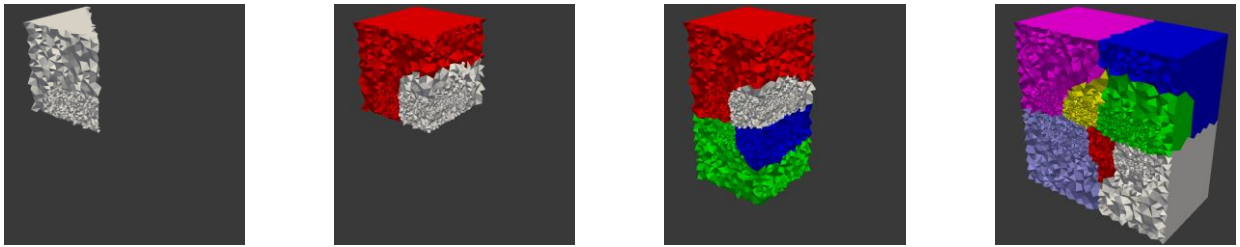
Parallelization Benchmark

- Weak scaling (doubling the problem size while doubling the resources)
- Strong scaling (keeping the problem size constant and doubling the resources)

Problem size

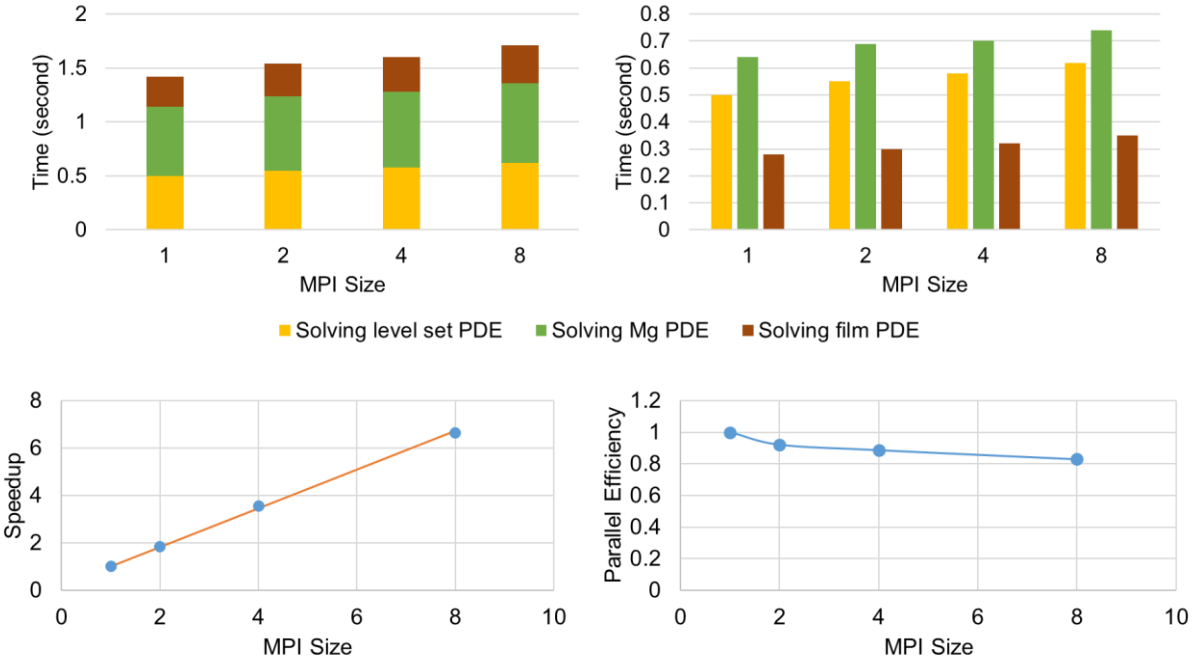


Mesh partitioned to available CPU cores

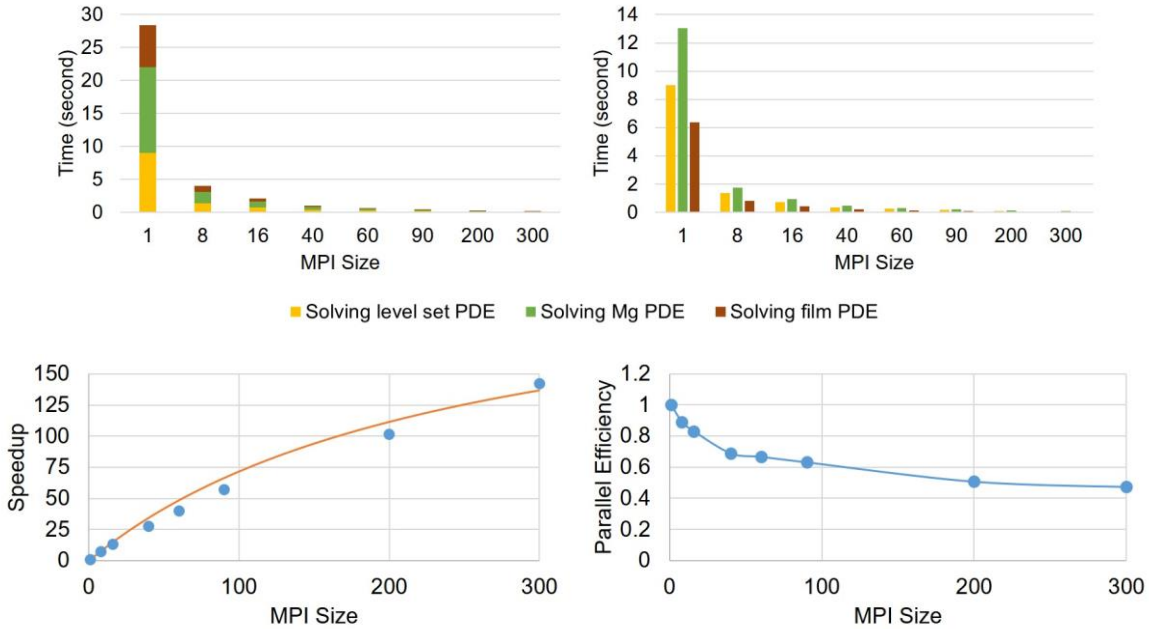


1 core | 2 cores | 4 cores | 8 cores

Weak Scaling Analysis

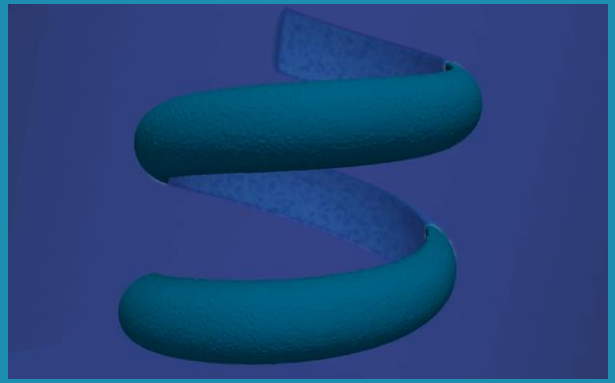


Strong Scaling Analysis



Conclusion

- A quantitative mathematical model to assess the degradation behavior of biodegradable metallic biomaterials
- Good agreement between the simulation predictions and experimentally obtained values for pH change
- The model can be an important tool to find the biodegradable metals properties and predict their biodegradation behavior



Thank you for your attention

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