High-performance simulation of biodegradation behavior of magnesium-based biomaterials

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Biodegradable Metals

- Mg, Zn, and Fe
- Great mechanical properties
- Biocompatibility and contribution in metabolism
- Potential applications:
  - Cardiovascular stents
  - Orthopedic implants

An Example in Orthopedics

- Osteoarthritis
- Hip Osteoarthritis
- Total hip replacement

(https://www.arthritis-health.com/types/osteoarthritis/videos)

So What Is The Problem?

- Problem:

  Tuning the degradation of the implant to the regeneration of the new bone

- Can be solved by:

  Building a mathematical framework for the assessment of biodegradation

(Source: 3D Systems Inc.)

Model Workflow

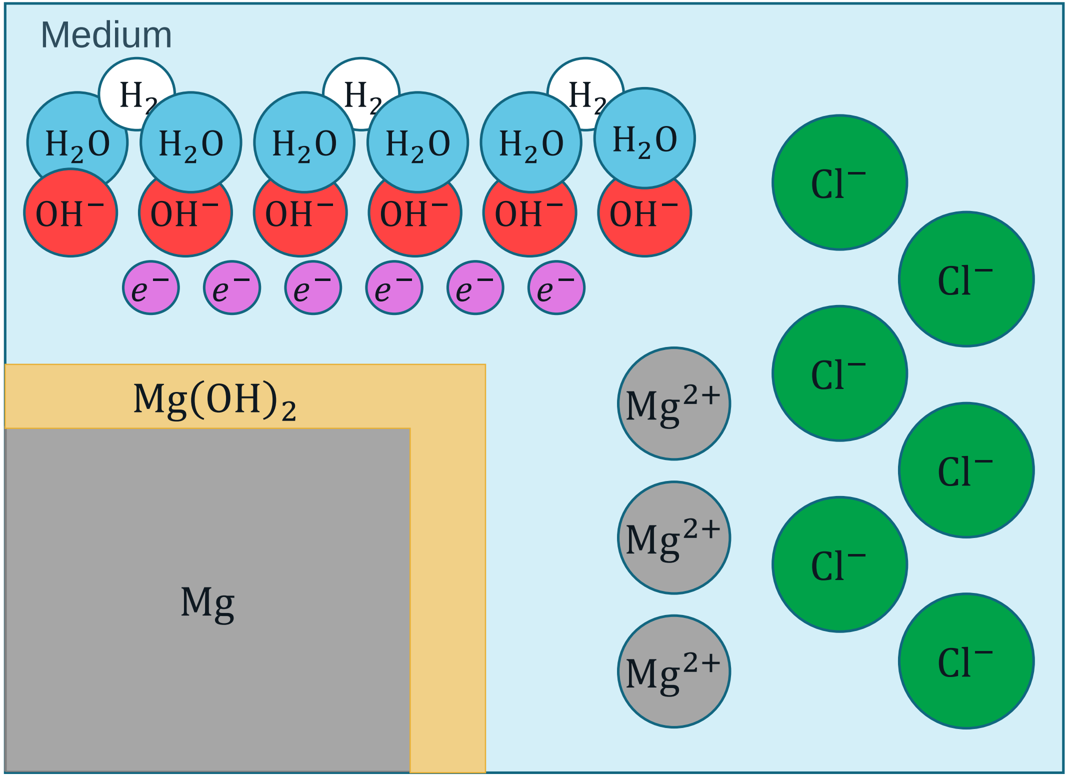
Underlying Science → **Mathematical Models** → **Computational Models**

Underlying Science
- Chemistry of biodegradation
- Physics of perfusion
- Biology of tissue growth

Mathematical Models
- Partial differential equations
- Reaction-Diffusion-Convection
- Level set method

Computational Models
- Finite difference method
- Finite element method
- Scientific computing libraries
- Open source solvers

Chemistry of Biodegradation



$$Mg \rightarrow Mg^{2+} + 2e^-$$

$$2H_2O + 2e^- \rightarrow H_2 + 2OH^-$$

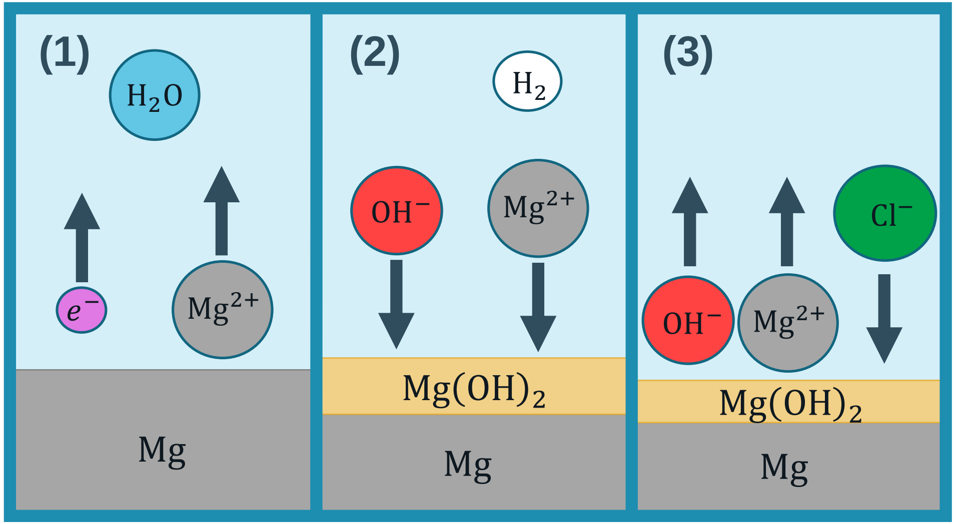
$$Mg^{2+} + 2OH^- \rightarrow Mg(OH)_2$$

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

Constructing Mathematical Model

The model captures:

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



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Mathematical Representation

Chemical reactions

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

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

Concentration notations

$$\mathrm{Mg^{2+}} \rightrightarrows [\mathrm{Mg}] \qquad \mathrm{Cl^-} \rightrightarrows [\mathrm{Cl}]$$

$$\mathrm{Mg(OH)_2} \rightrightarrows [\mathrm{Film}]$$

Derived PDEs

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

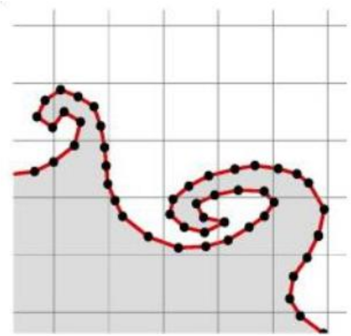
$$\frac{\partial[\mathrm{Film}]}{\partial t} = k_1[\mathrm{Mg}]\left(1 - \frac{[\mathrm{Film}]}{[\mathrm{Film}]_{\mathrm{max}}}\right) - k_2[\mathrm{Film}][\mathrm{Cl}]^2$$

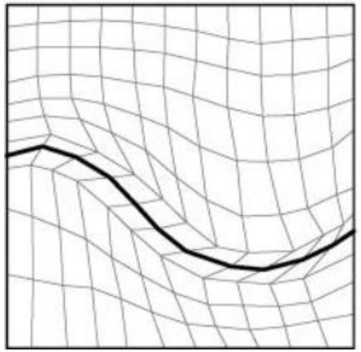
$$\frac{\partial[\mathrm{Cl}]}{\partial t} = \nabla.\left(D^e_{\mathrm{Cl}}\nabla[\mathrm{Cl}]\right)$$

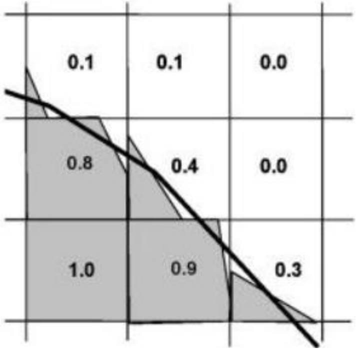
$$\left([\mathrm{Film}]_{\mathrm{max}} = \rho_{\mathrm{Mg(OH)_2}} \times (1-\epsilon)\right)$$

Identifying Moving Biodegradation Interface

- Different approaches:
  1. Interface tracking methods
  2. Interface fitting methods
  3. Interface capturing methods

1) 

2) 

3) 

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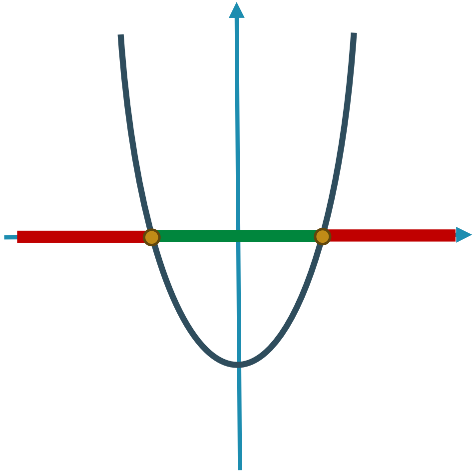
Interface Capturing using Implicit Interfaces

- Implicit interfaces can be defined by an implicit distance function

1D implicit function $\phi(x) = x^2 - 2$

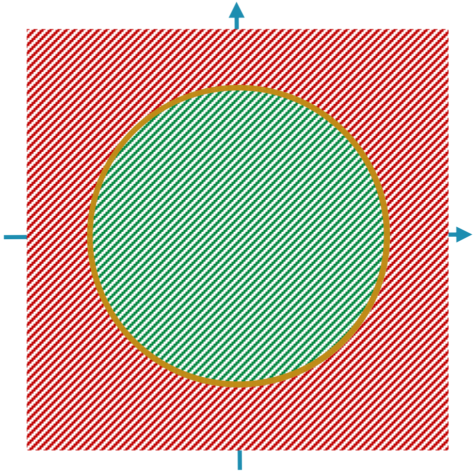


$\phi = 0$
interface

$\phi > 0$
outside

$\phi < 0$
inside

2D implicit function $\phi(x, y) = x^2 + y^2 - r^2$



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Level Set Method

- A PDE to capture the moving implicit surface
- $\phi = \phi(x, y, z, t)$

$$\frac{\partial \phi}{\partial t} + \cancel{\underbrace{\vec{V}\nabla\phi}_{\text{External velocity field}}} + \underbrace{\mathrm{v}|\nabla\phi|}_{\text{Normal direction motion}} = \cancel{\underbrace{b\kappa|\nabla\phi|}_{\text{Curvature-dependent term}}}$$

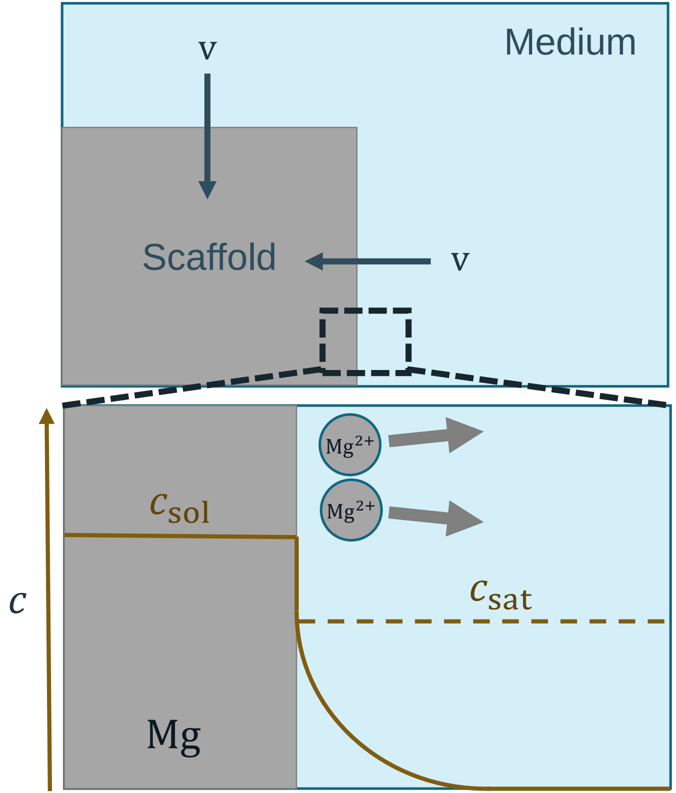
Level Set Method for Biodegradation

Level set: $$\frac{\partial \phi}{\partial t} + \mathrm{v}|\nabla \phi| = 0$$

Rankine-Hugoniot: $$\{\mathbf{J}(x,t) - (c_{\mathrm{sol}} - c_{\mathrm{sat}})\mathrm{v}(x,t)\}.n = 0$$

Mg scaffold: $$D^{e}_{\mathrm{Mg}} \nabla_n [\mathrm{Mg}] - ([\mathrm{Mg}]_{\mathrm{sol}} - [\mathrm{Mg}]_{\mathrm{sat}})\mathrm{v} = 0$$

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



Constructing Computational Model

- Not feasible to implement models in commercial software packages
- Discretizing PDE equations, numerical computation
  - Finite difference method (temporal terms)
  - Finite element method (spatial terms)

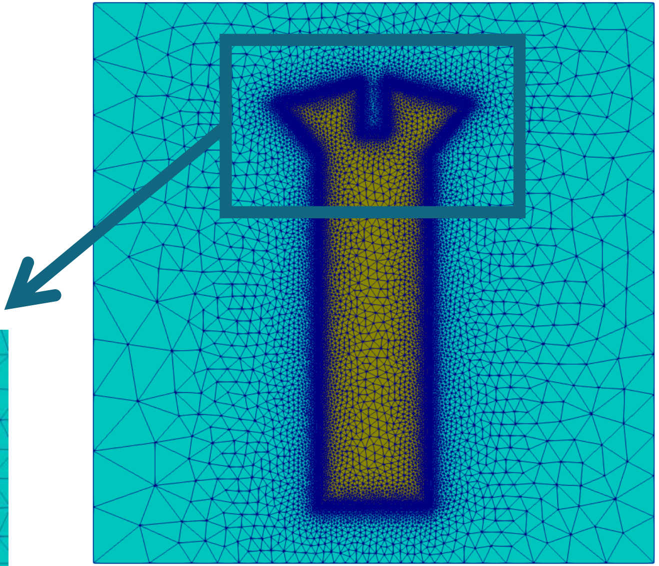
$$\frac{\partial[\mathrm{Mg}]}{\partial t} = \nabla.\left(D_{\mathrm{Mg}}^{e}\nabla[\mathrm{Mg}]\right) - k_1[\mathrm{Mg}]\left(1 - \frac{[\mathrm{Film}]}{[\mathrm{Film}]_{\mathrm{max}}}\right) + k_2[\mathrm{Film}][\mathrm{Cl}]^2$$

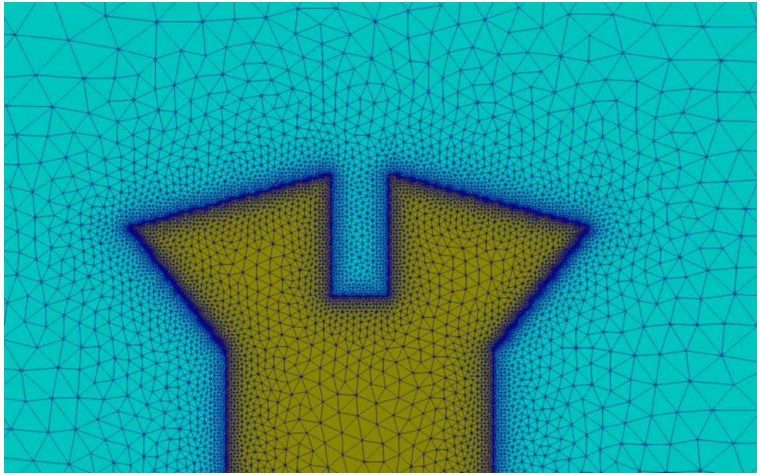
Implicit backward Euler

1st order Lagrange polynomial as the basis function

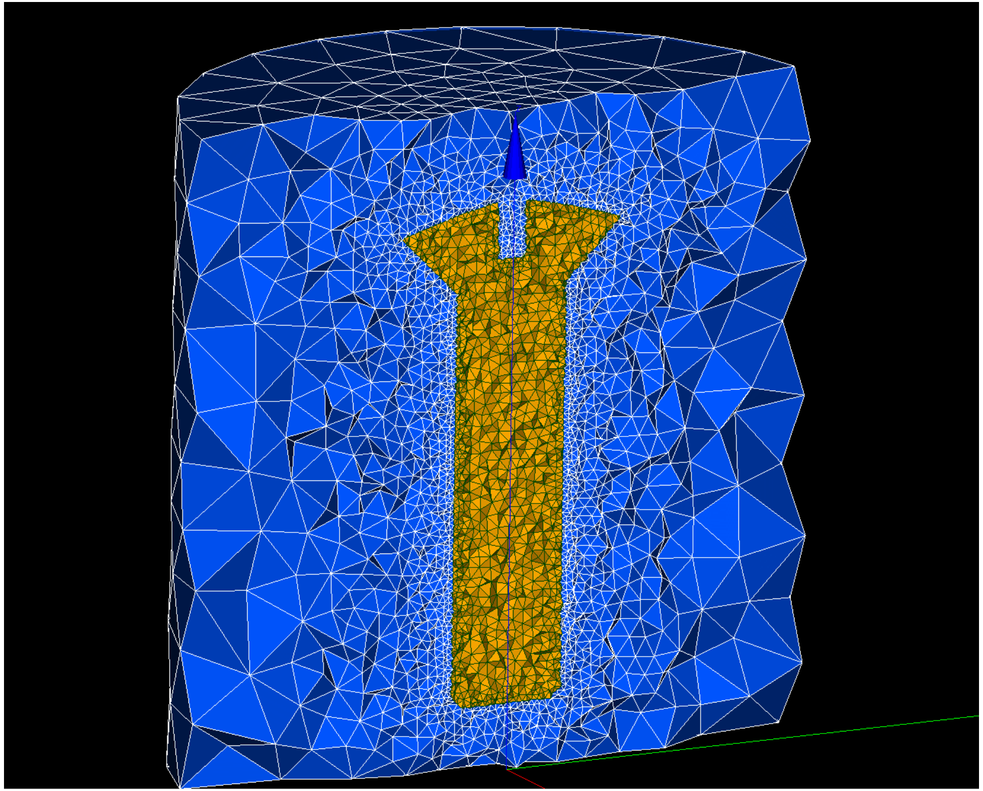
Computational Mesh

- Euler Mesh
- High accuracy in the interface
- Refining the mesh adaptively





An Example of 3D Mesh



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Implementing Computational Model

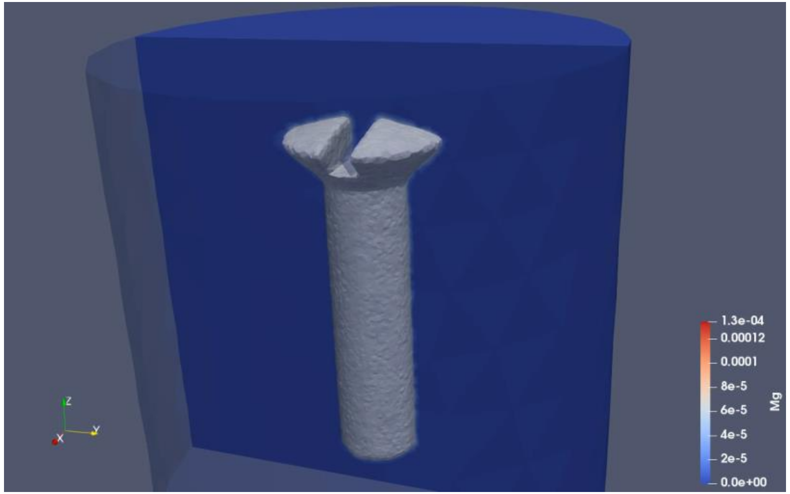
- Mesh generation (SALOME, TetGen)
- Weak form implementation (FreeFem++)
- Parallelization
  - Message Passing Interface (MPICH)
  - High-performance Domain Decomposition (HPDDM)
  - High-performance solvers (MUMPS, PETSc)

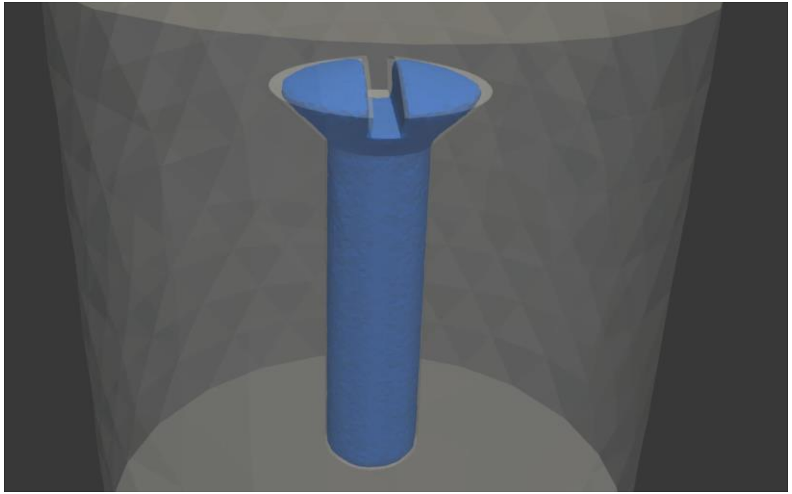
A typical 3D simulation:
#Elements ~= 800,000
#DOF ~= 500,000

Verification of the code

Verifying the correct behavior of:

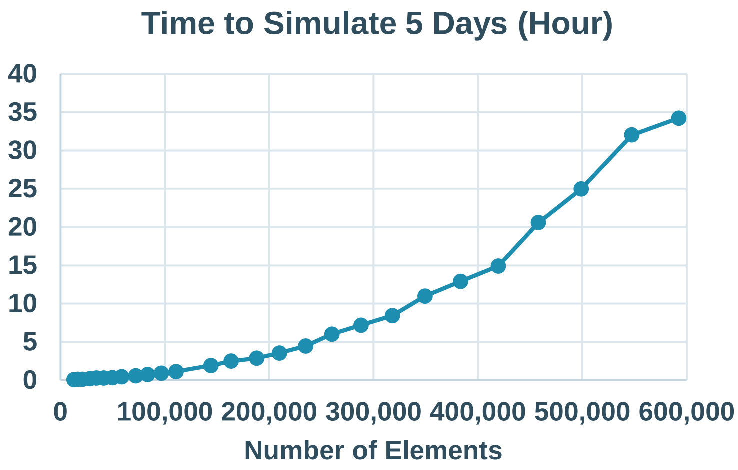
- Mass transfer and ion release
- Level set surface tracking

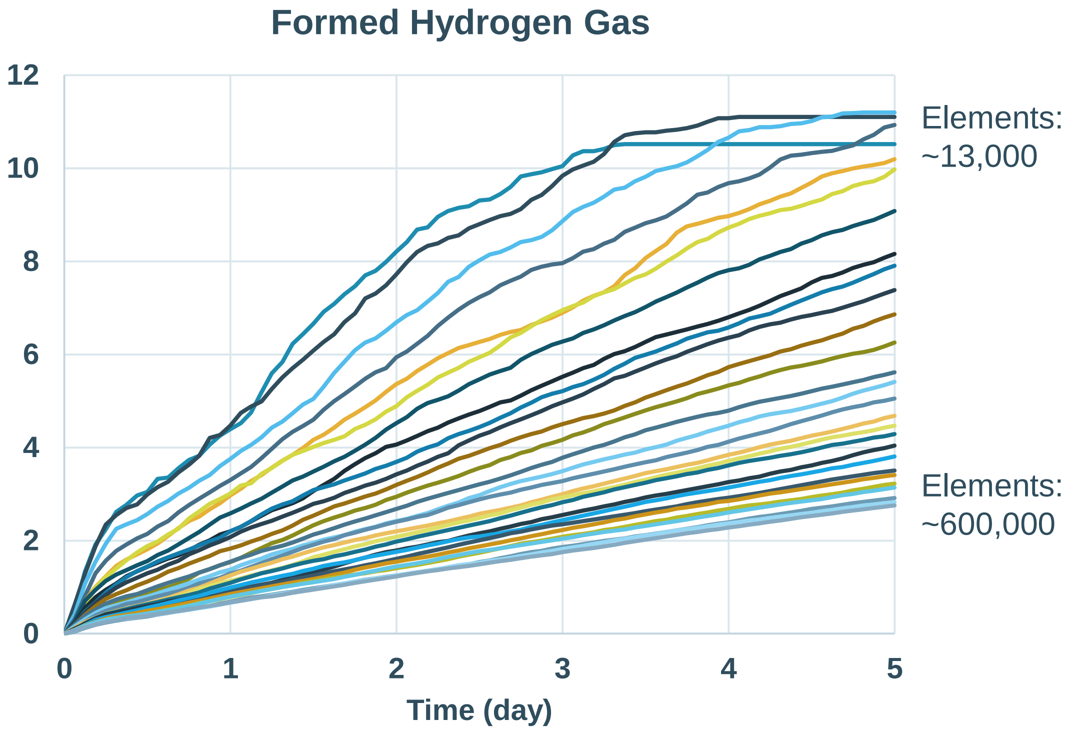




Convergence Studies

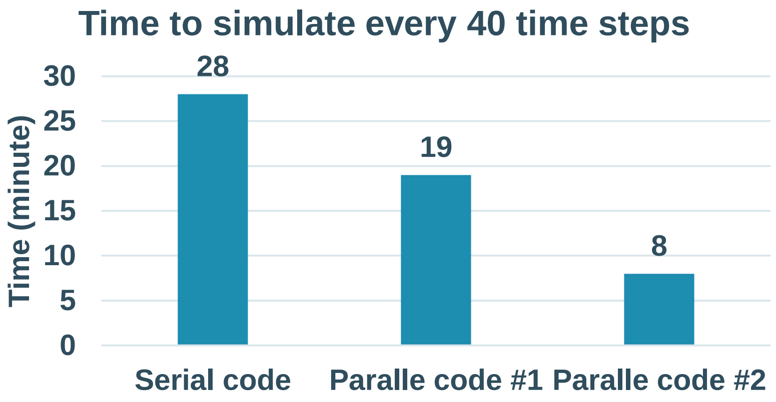
- Mesh and time step sensitivity
- Crucial for in-house codes



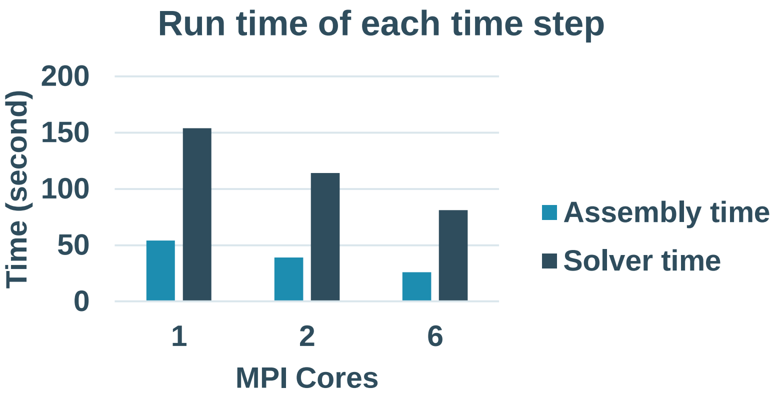


Benchmarking parallelization

- Serial and parallel code should produce the same result
- Evaluating scale-up



(DOF: 44,663, MPI Cores: 4)



(DOF: 381,205, Elements: 2,233,524, MPI Cores: 4)

Calibration of the Model

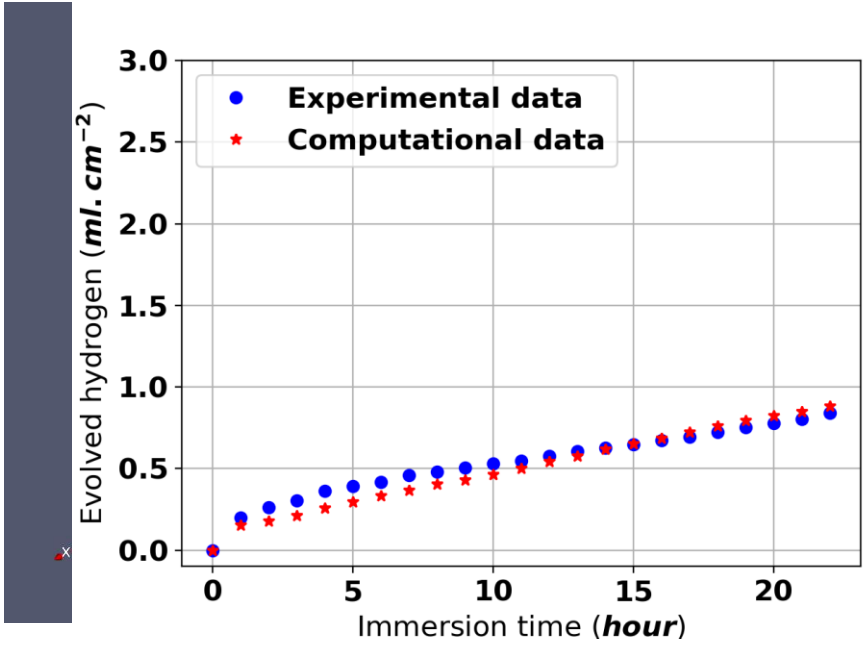
- Different approaches to calibrate models
  - Mass loss
  - Formed hydrogen gas
- Obtaining reaction rates and diffusion coefficients

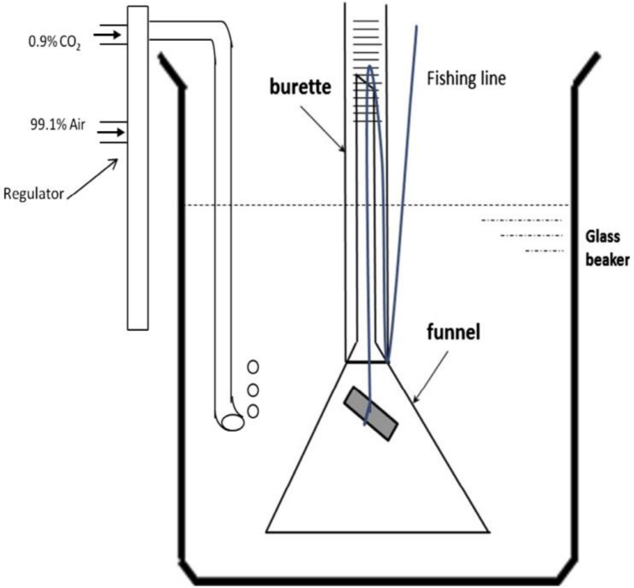
$$\frac{\partial[\mathrm{Mg}]}{\partial t} = \nabla.\left(D_{\mathrm{Mg}}^{e}\nabla[\mathrm{Mg}]\right) - k_1[\mathrm{Mg}]\left(1 - \frac{[\mathrm{Film}]}{[\mathrm{Film}]_{\mathrm{max}}}\right) + k_2[\mathrm{Film}][\mathrm{Cl}]^2$$

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

$$\frac{\partial[\mathrm{Cl}]}{\partial t} = \nabla.\left(D_{\mathrm{Cl}}^{e}\nabla[\mathrm{Cl}]\right)$$

Experimental Data and Model Calibration

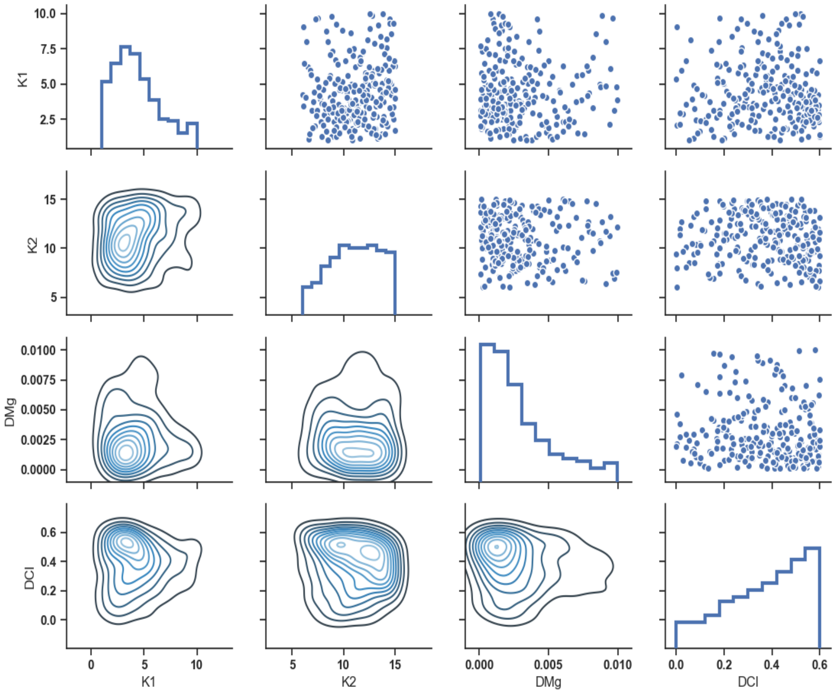




(Abidin et al., Corrosion Science, 2013)

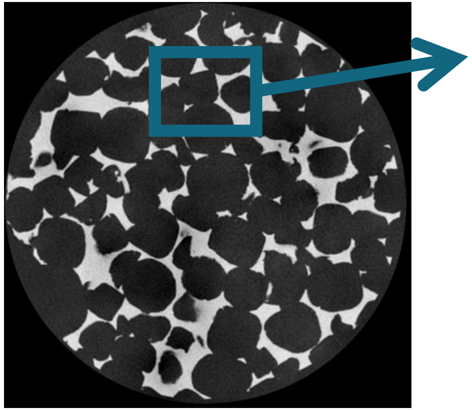
Model Parameters Estimation

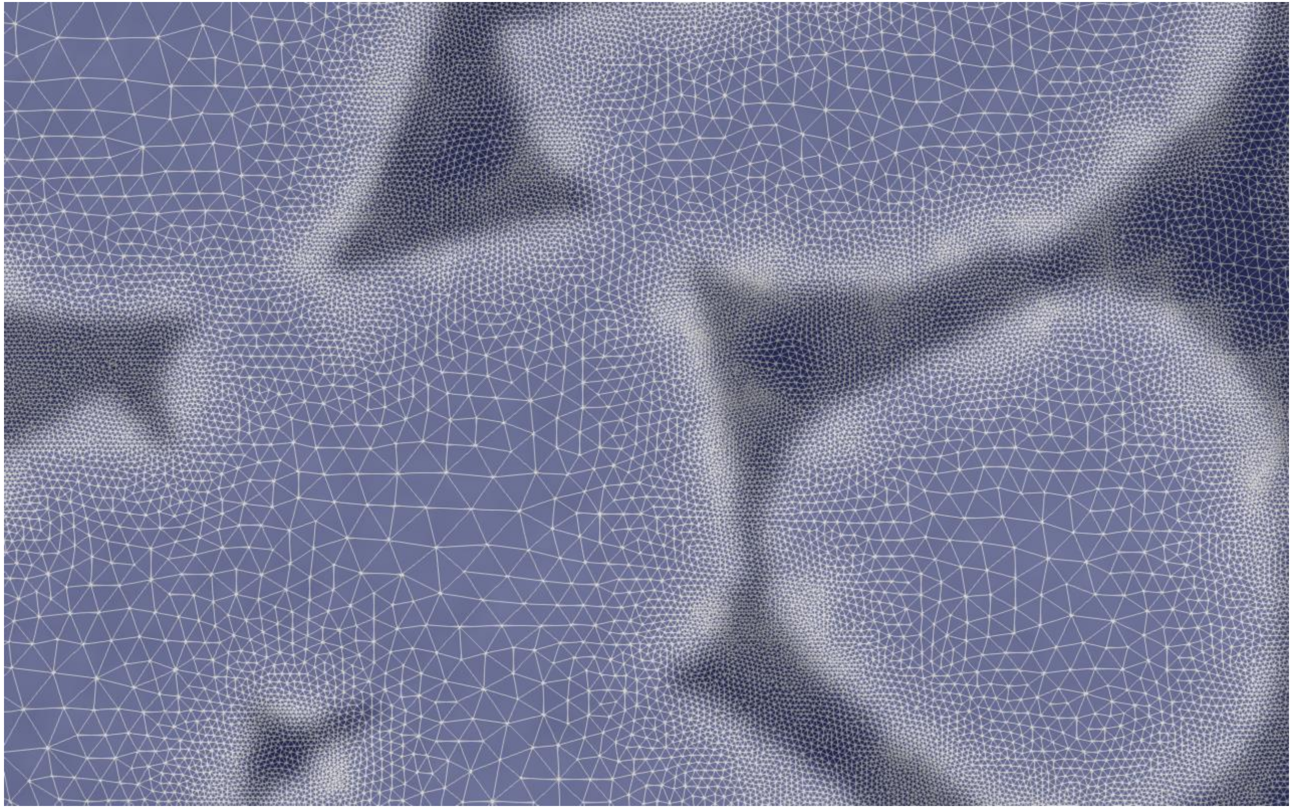
- Each simulation takes ~8 hours to run
- Using a Bayesian optimization algorithm
- Cost function is the RMSE of difference in experimental data and model output



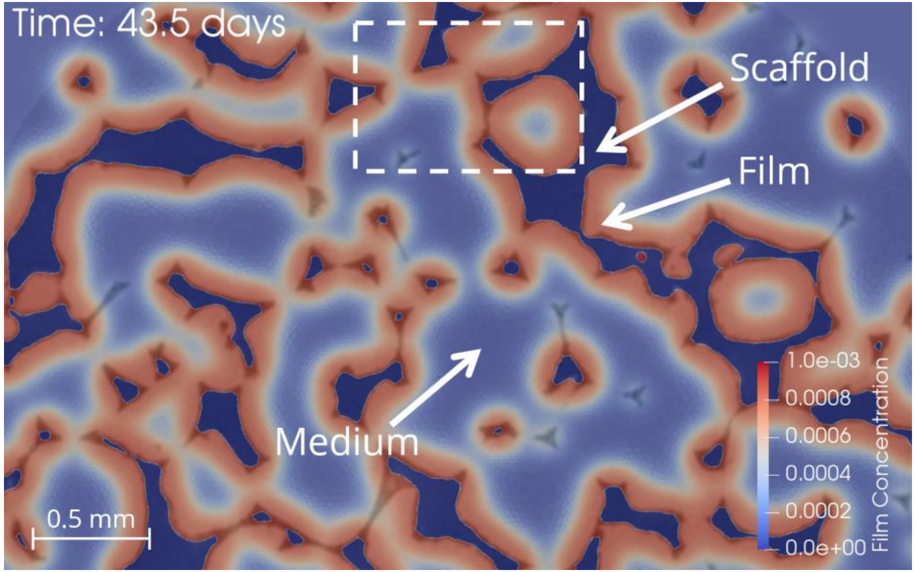
Application for Porous Scaffolds

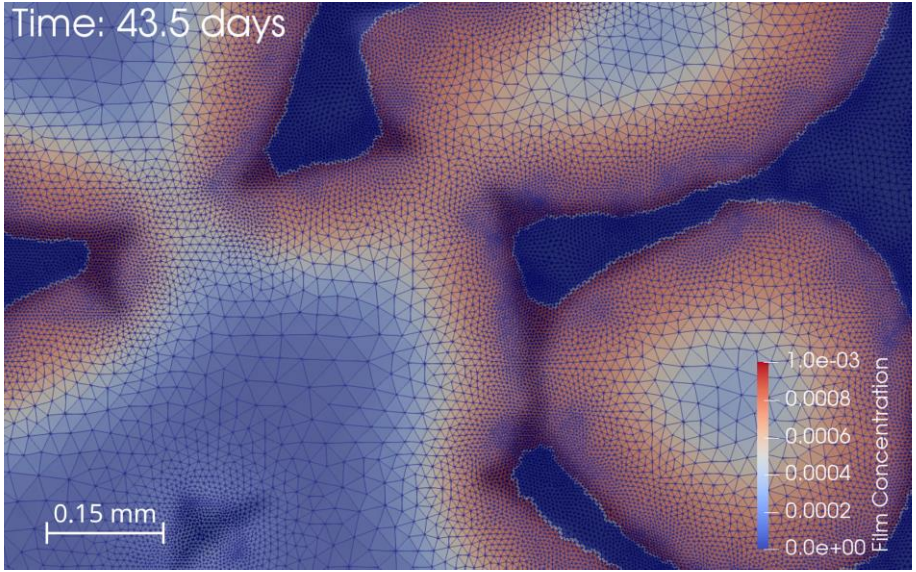
- Sample mesh based on a CT image of a porous Mg scaffold





2D Mg Scaffold – Film Formation





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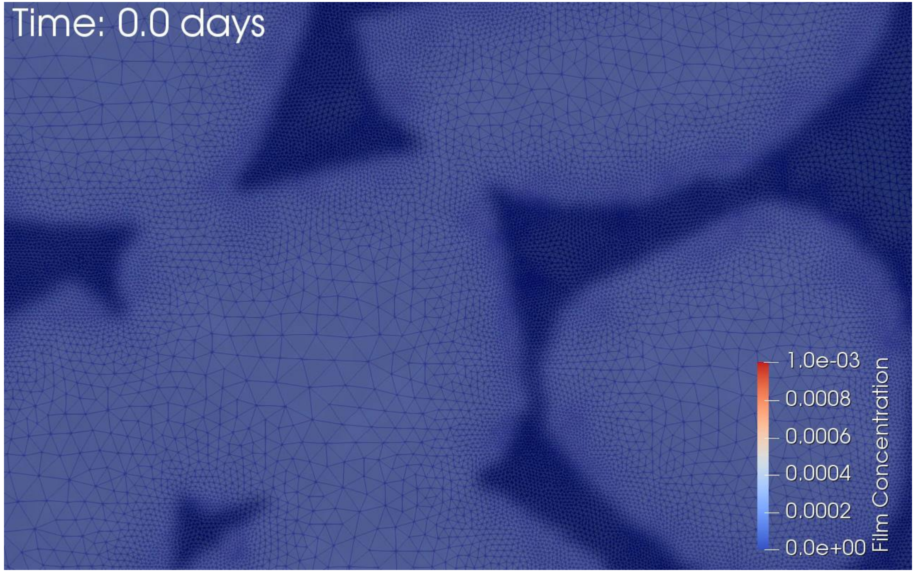
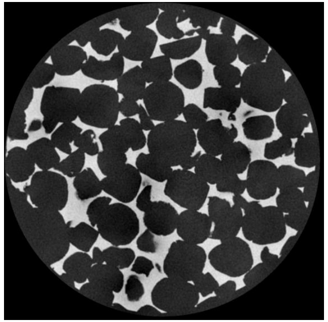
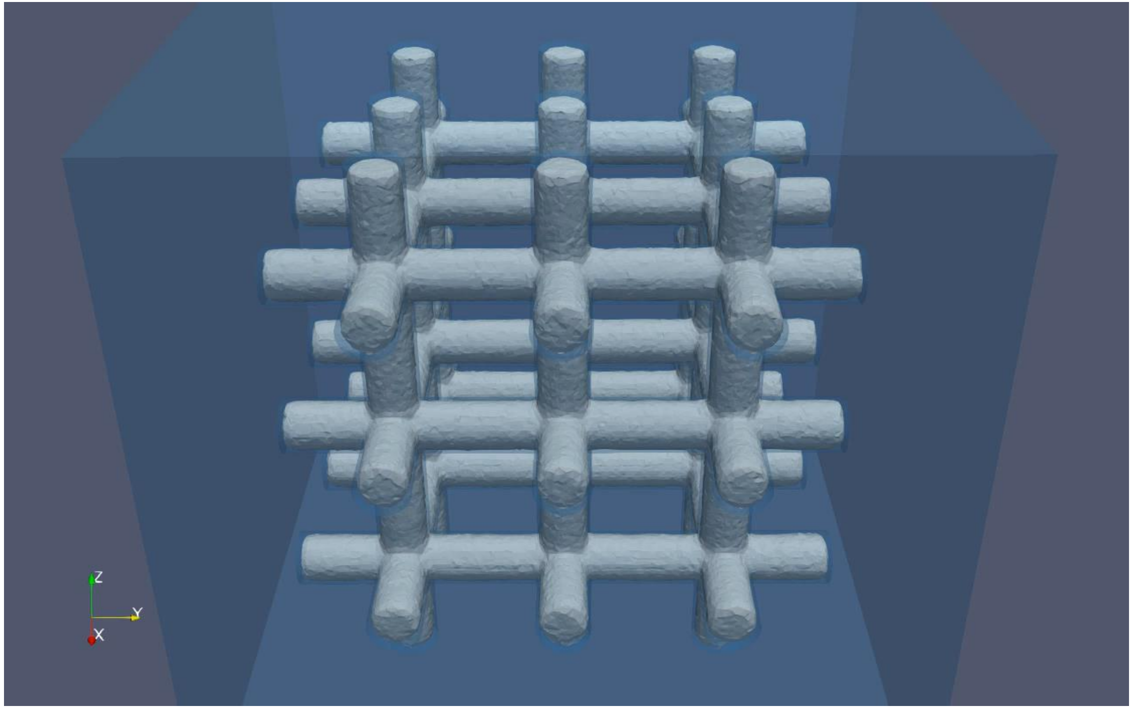
2D Mg Scaffold – Film Formation



2D Mg Scaffold – Film Formation



3D Porous Scaffold Degradation



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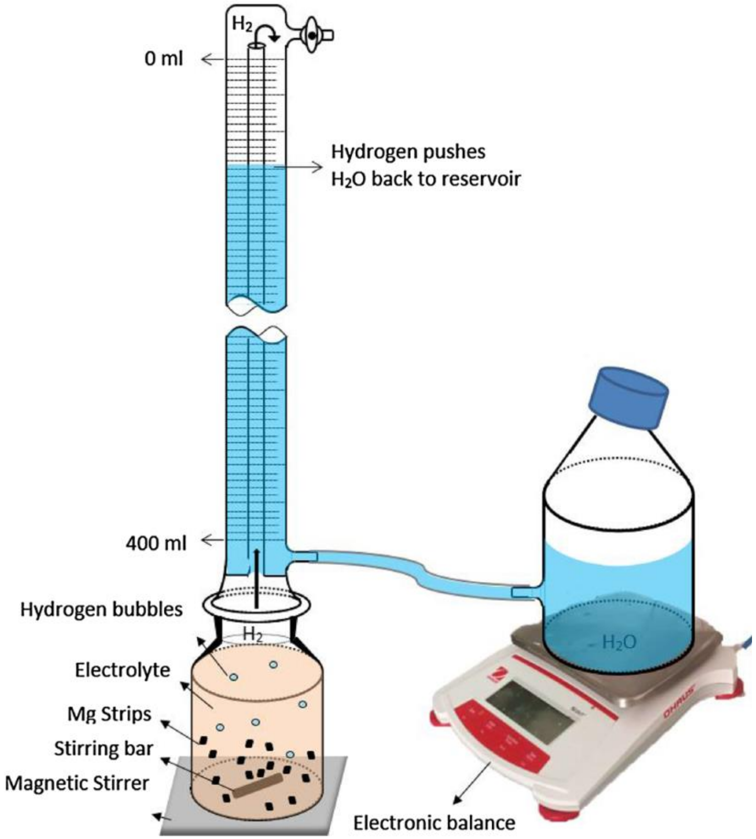
Model Validation

- Validation is currently taking place
- We use another experimental setup to validate the model
- Models will be extended to capture pH changes, and that will be used for model validation



(Mei et al., Corrosion Science, 2019)

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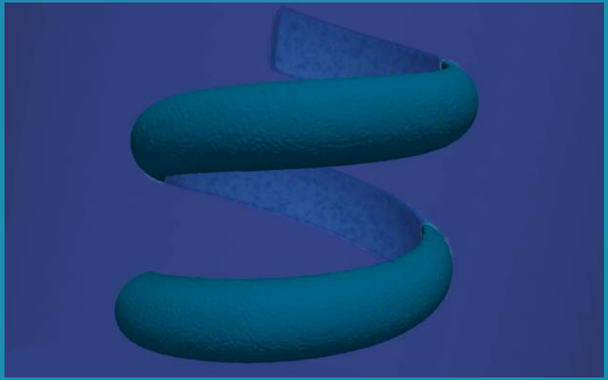
Conclusion

- A quantitative mathematical model to assess the degradation behavior of biodegradable metallic implants in-silico
- Once fully validated, the model will be an important tool to find the right design and properties of the magnesium-based implants



Thank you for your attention

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