Computational modeling of in-vitro biodegradation of metallic scaffolds and bone implants

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Biodegradable Metals

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

Background

- Acetabular implants
- Total hip replacement
- Considering biodegradation behavior beside optimizing mechanical stability

(Source: 3D Systems Inc.)

Problem Definition

- Implants should be removed at the end of their lifetime
- Some extra bone is also removed along with the implant
- Making at least part of the implant from biodegradable materials

(Source: 3D Systems Inc.)

Objective

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

Model Workflow

Underlying Science

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

Mathematical Models

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

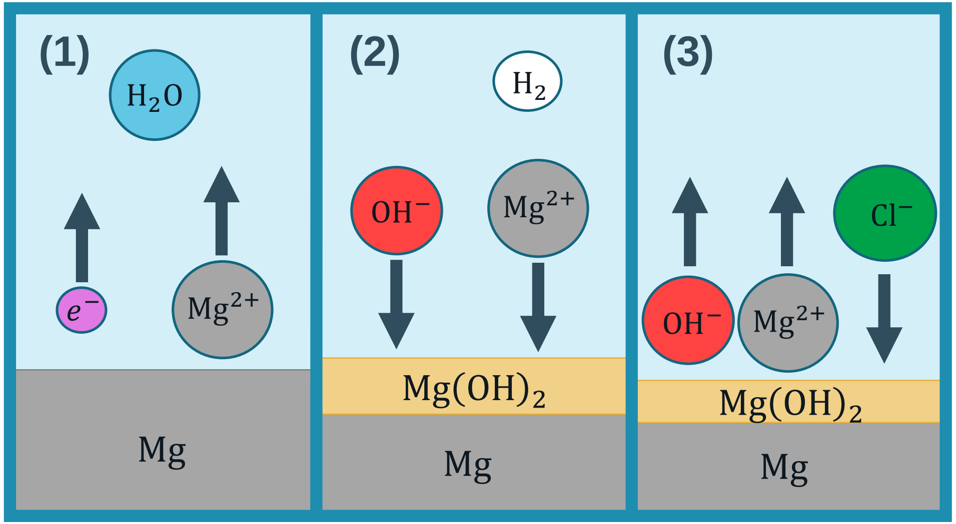
Computational Models

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

Chemistry of Biodegradation

The model captures:

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



Mathematical Representation

Chemical reactions

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

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

Derived Partial Differential Equations

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

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

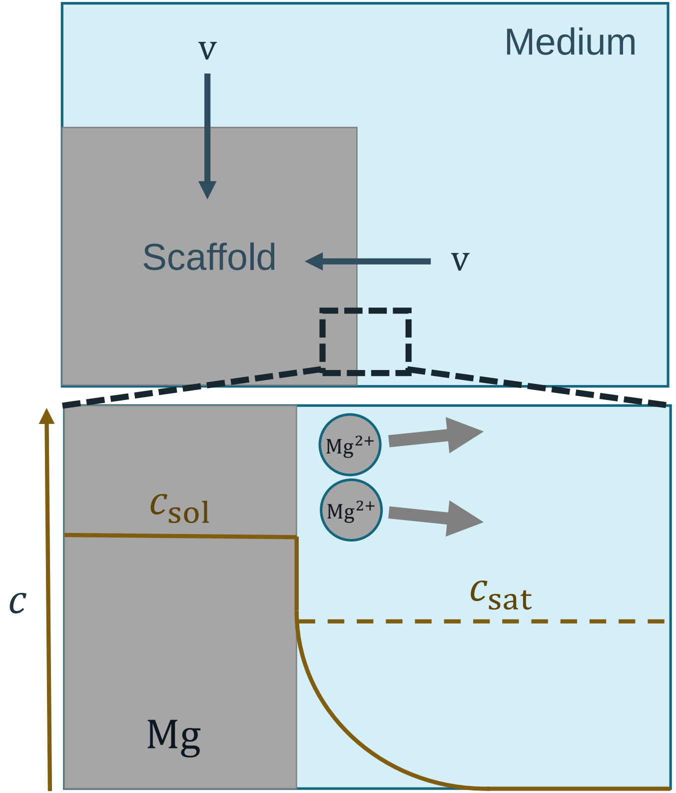
$$\frac{\partial C_{\mathrm{Cl}}}{\partial t} = \nabla.\left(D^e_{\mathrm{Cl}} \nabla C_{\mathrm{Cl}}\right)$$

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

Capturing the Biodegradation Interface

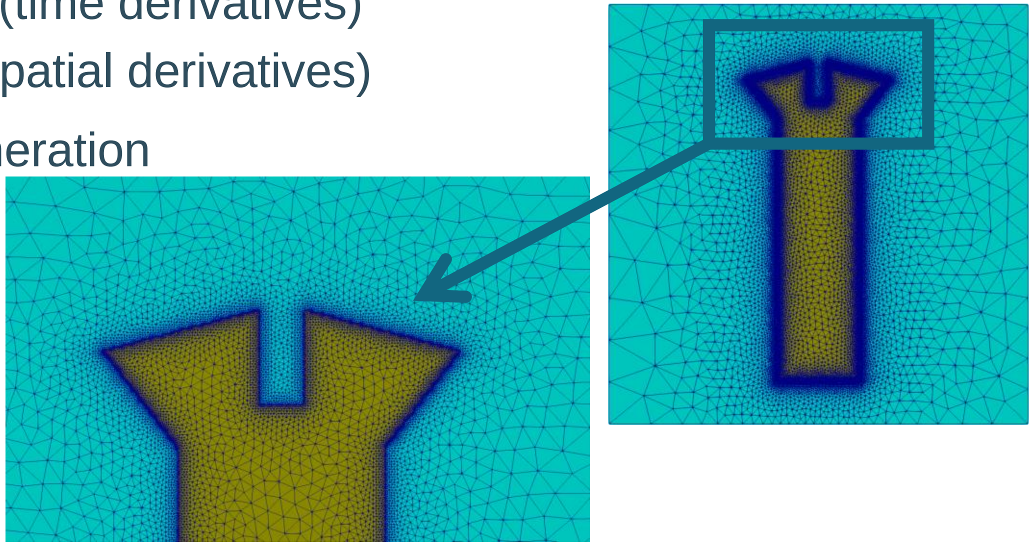
- Implicit moving interface tracking
- Level set method

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



Constructing Computational Model

- Not feasible to implement models in sophisticated software packages
- Discretizing PDE equations, numerical computation
  - Finite difference method (time derivatives)
  - Finite element method (spatial derivatives)
- Adaptively refined mesh generation

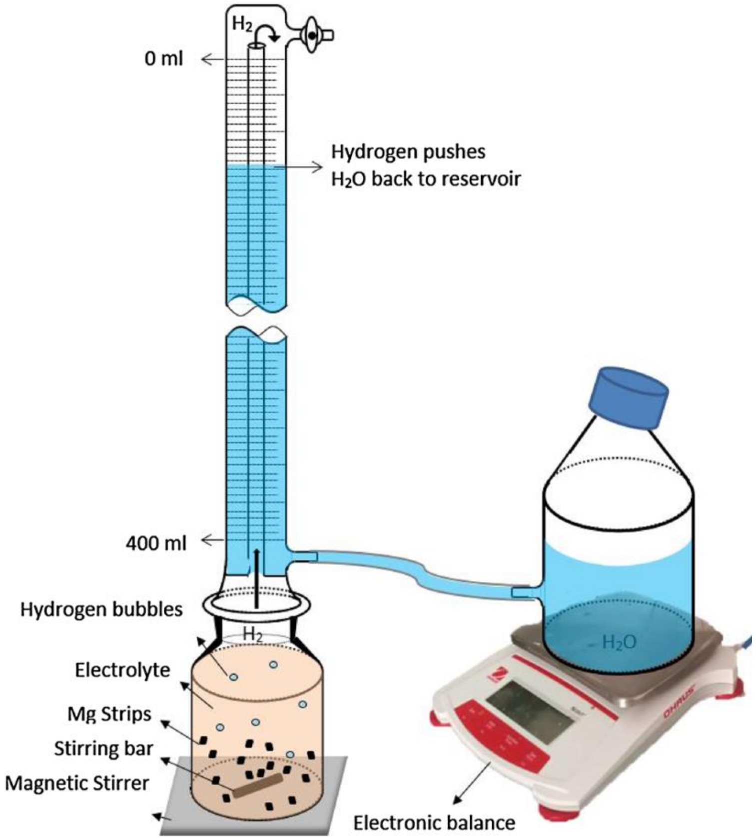


Implementing Computational Model

- Mesh generation (SALOME, GMSH)
- Weak form implementation (FreeFEM)
- Parallelization
  - High-performance Domain Decomposition (HPDDM)
  - High-performance preconditioners and solvers (PETSc)

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)

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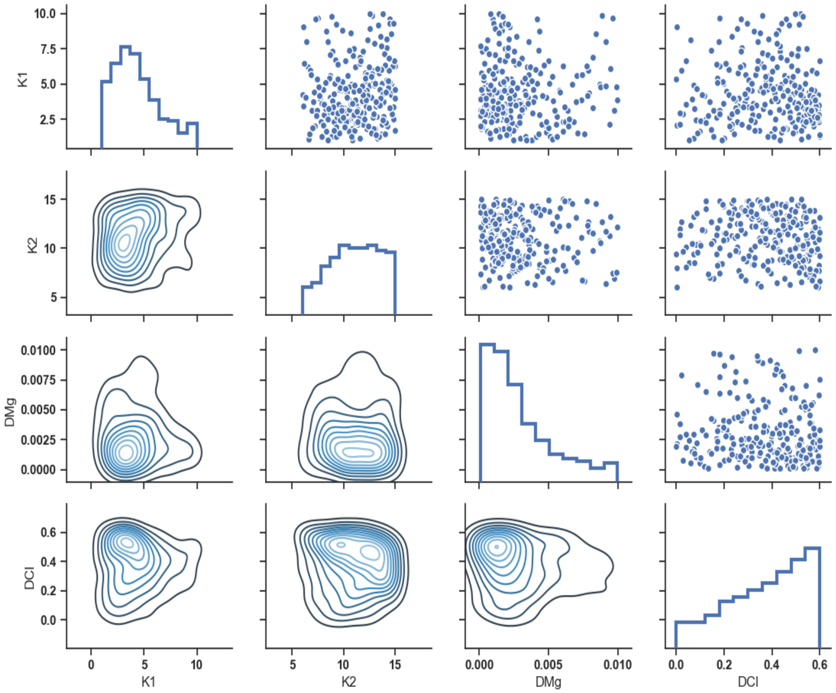
Model Parameters Estimation

- Sensitivity analysis to get the important parameters in different diffusion regimes
- Using a Bayesian optimization algorithm for estimating the effective parameters



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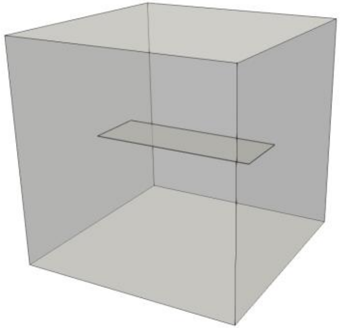
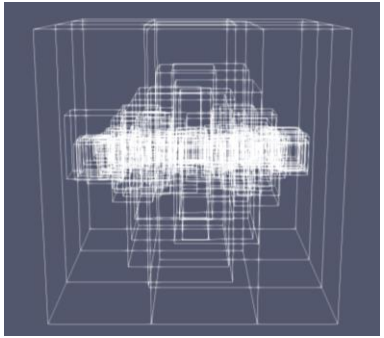
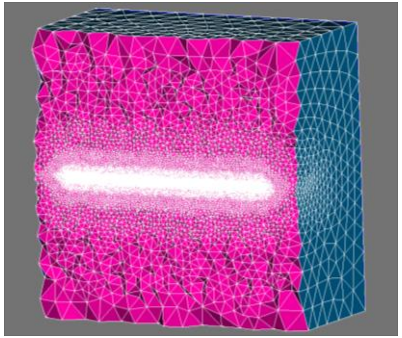
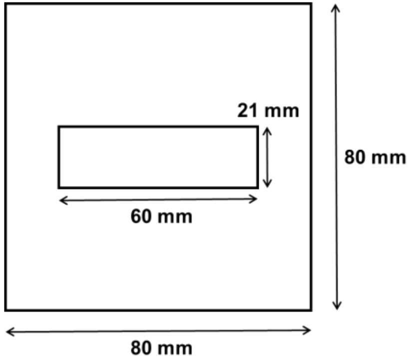
Simulation Setup

- 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

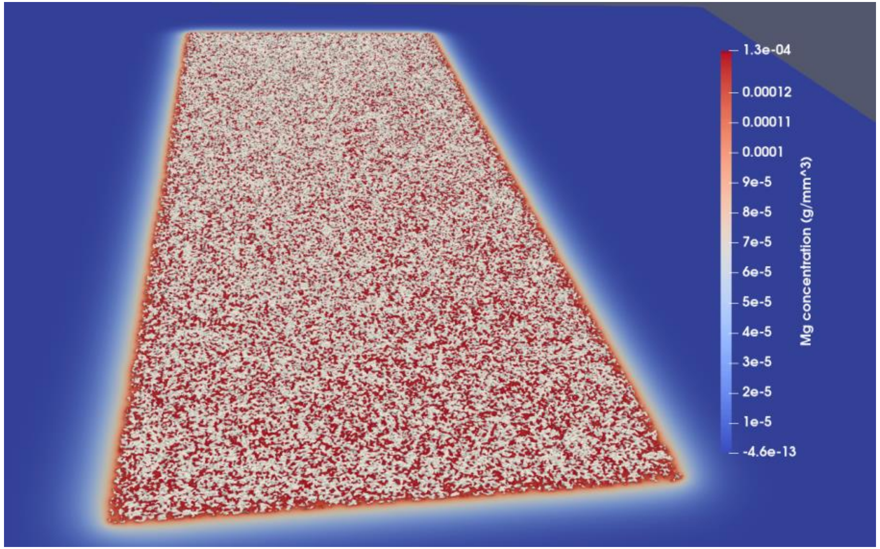




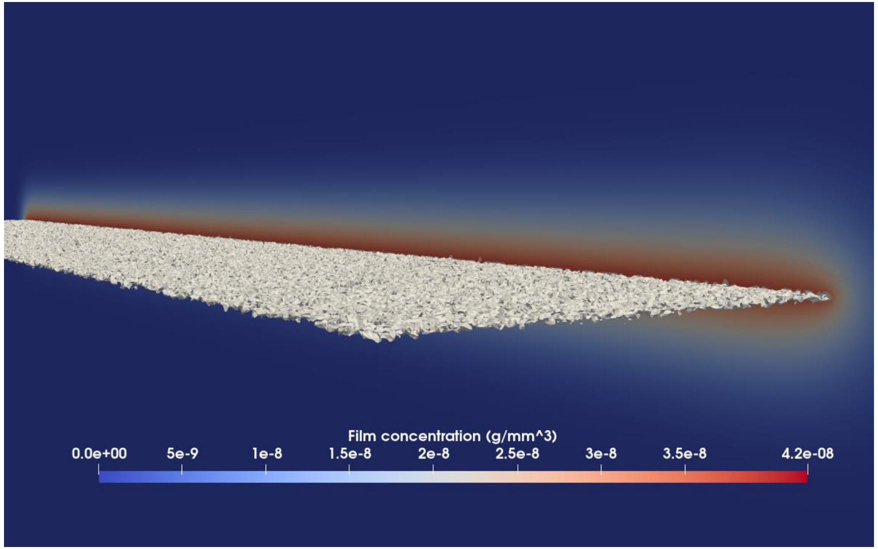




Simulation Results - Degradation

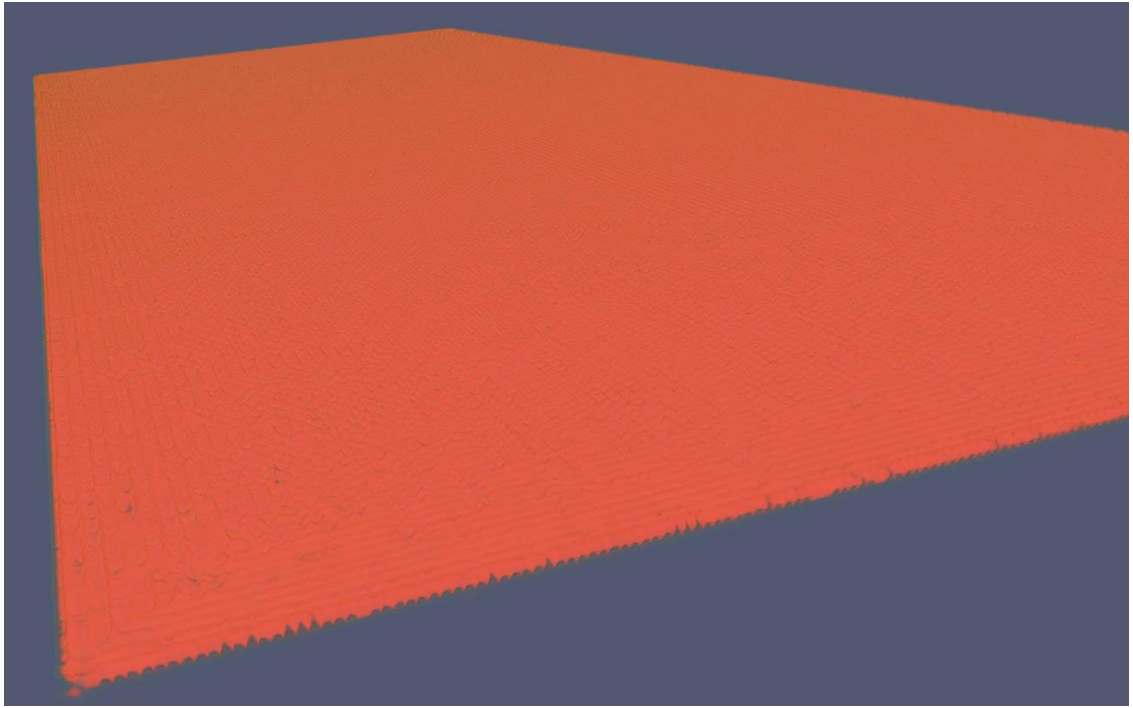


Release of Mg ions

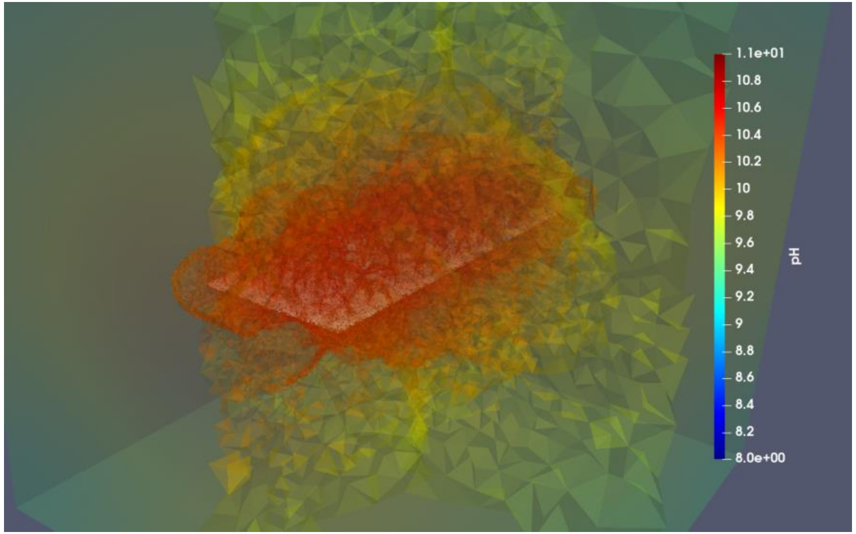


Formation of the protective film

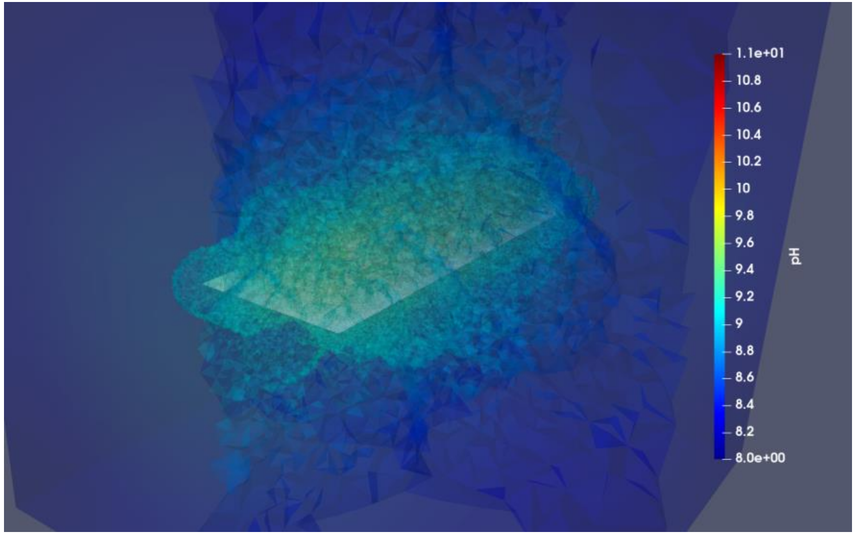
Simulation Results - Degradation



Simulation Results - pH Change

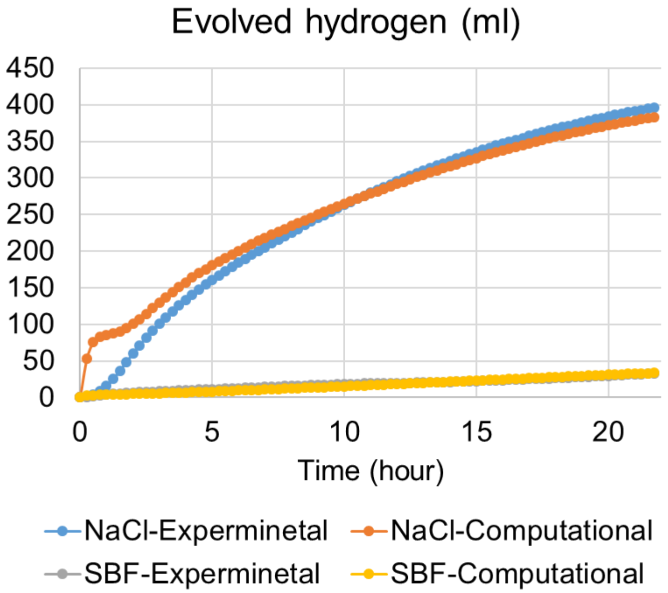


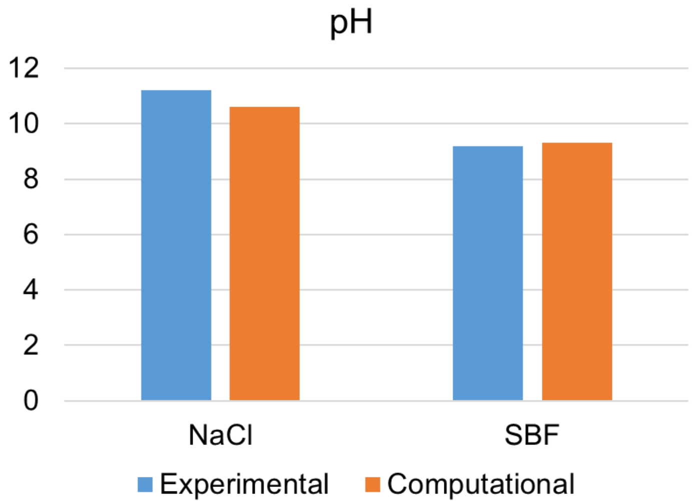
High diffusion (NaCl solution)



Low diffusion (SBF solution)

Quantitative Results





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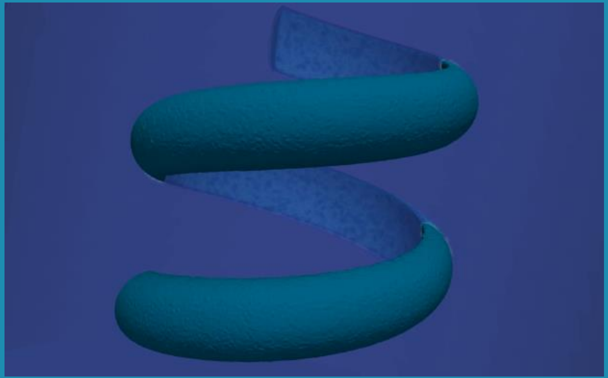
Conclusion

- A quantitative mathematical model to assess the degradation behavior of biodegradable metallic implants in-silico
- The model can be an important tool to find the biodegradable metals properties and predict the biodegradation behavior of implants that improves current workflows of designing them



Thank you for your attention

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