Physics-Informed Neural Network Model for Cell Viability and Oxygen Consumption of Pancreatic Islets

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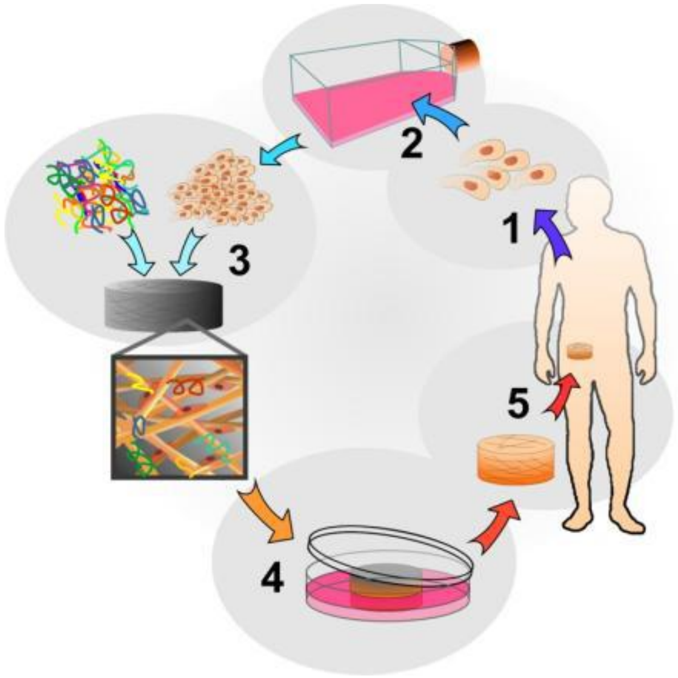
Tissue Engineering

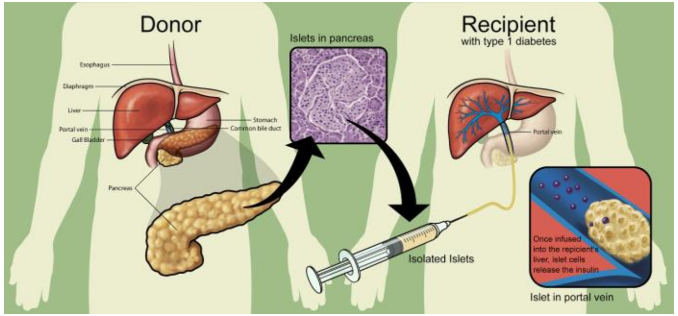
- An interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function or a whole organ (Langer & Vacanti, 1994)
- Cell, carrier, and growth factors

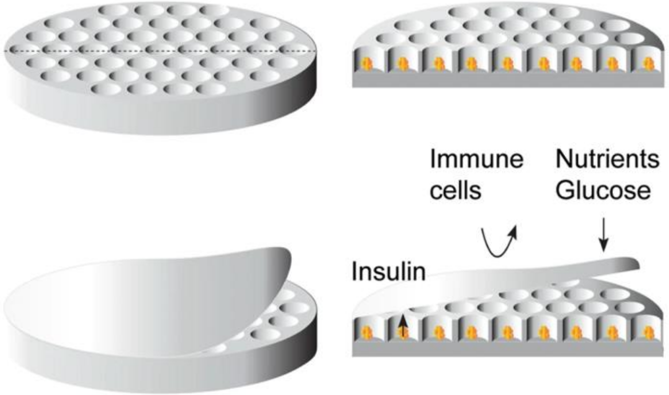


(source: J.H. George)

Pancreatic Islets Transplantation

- Islet transplantation to treat type 1 diabetes
- Proper preparation in a culturing process
- Viability of cultured islets is limited by hypoxia (death due to lack of vascularization and oxygen)
- Pancreatic islets are vulnerable due to large size
- Putting islets into micro-devices inside wells for gradient-driven oxygen diffusion





(sources: M.A. Naftanel et al., 2004, and K. Skrzypek et al., 2017)

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Problem Definition

- Challenge:
  - Tuning the culture device such that it prevents hypoxia
- Can be solved by:
  - Mathematical modeling of oxygen supply and consumption
  - Coupling oxygen transport models with vascularization models
  - Simulating the models by solving the transient mathematical equations

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Modeling Workflow

Underlying Phenomena → **Mathematical Models** → **Computational Models**

Underlying Phenomena	**Mathematical Models**	**Computational Models**
Oxygen consumption/supply	Partial differential equations	Finite element method
Hypoxia	Reaction-Diffusion-Convection	Physics-informed neural networks
Vascularization	Navier-Stokes equations	

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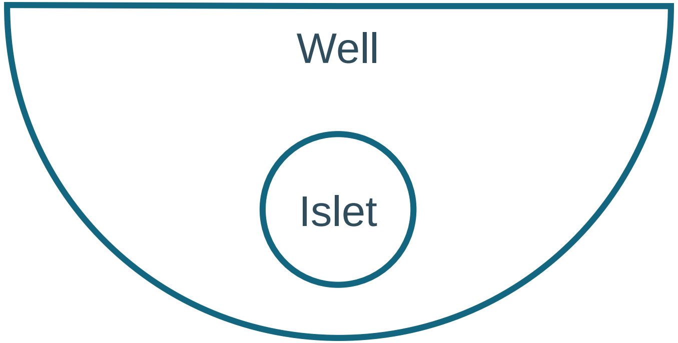
Constructing Mathematical Model

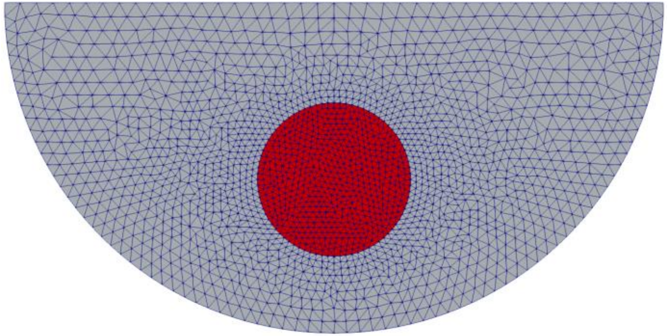
- Converting the biological phenomena into mathematical forms
- Reaction-diffusion-convection partial differential equations (PDE)
- Oxygen transport equation:

$$\frac{\partial C_{\mathrm{O_2}}}{\partial t} = \underbrace{\nabla.\left(D\nabla C_{\mathrm{O_2}}\right)}_{\text{Diffusion}} - \underbrace{\nabla.\left(\mathbf{u}C_{\mathrm{O_2}}\right)}_{\text{Convection}} + \underbrace{R_{\mathrm{max,O_2}} \frac{C_{\mathrm{O_2}}}{C_{\mathrm{O_2}} + C_{\mathrm{MM,O_2}}} . \varphi \frac{C_{\mathrm{gluc}}}{C_{\mathrm{gluc}} + C_{\mathrm{MM,gluc}}} . \delta\left(C_{\mathrm{O_2}} > C_{\mathrm{cr}}\right)}_{\text{Reaction}}$$

Implementing Computational Model

- Constructing the geometry
- Discretizing PDEs, finite element method
- Various techniques to linearize equations:
  - Picard-relaxation
  - Newton
- Requires a mesh to begin with
- Non-linear equations can become a problem





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Alternative Technique for Solving PDEs

- Commonly-used techniques: finite element and finite difference methods
- Approximating the derivative terms and variational formulation
- What if we employ some techniques from machine learning (ML)?
- Embedding the physics into the ML model
- Physics-informed neural networks (PINN)

Why Physics-Informed Neural Networks?

- Handshaking of HPC and AI for mechanistic modeling
- Dealing with nonlinearity
- Easier parameterization
- Enhanced inverse problems formulation
- PDE-constrained optimization
- Extensibility

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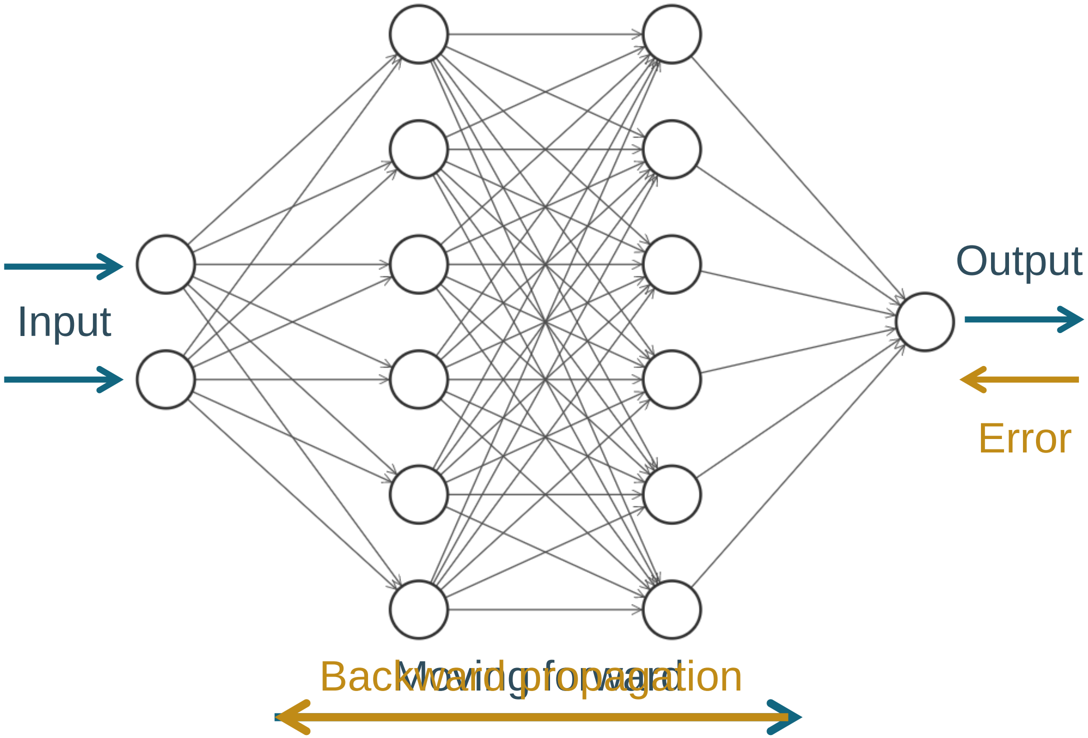
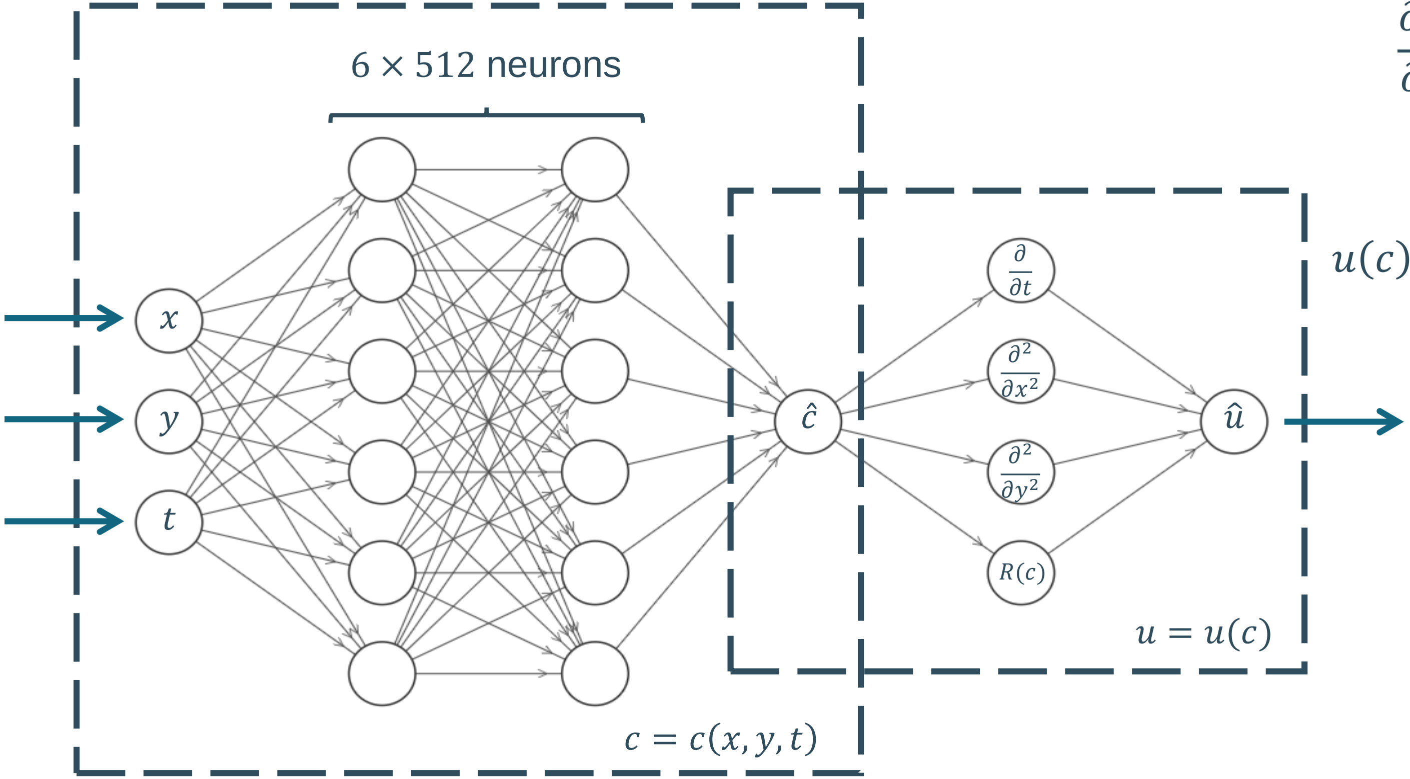
Core Idea of PINN Models

- PINN models are deep neural network (NN) models in supervised learning
- Approximating functions using NN models
- By automatic differentiation, the derivatives of the function can be approximated



Solving PDEs Using PINN Models



$$\frac{\partial c}{\partial t} = \nabla.(D\nabla c) + R(c)$$

$$c = c(x, y, t)$$

$$u(c) = \frac{\partial c}{\partial t} - \nabla.(D\nabla c) - R(c)$$

$$u(c) = 0$$

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Training PINN Models

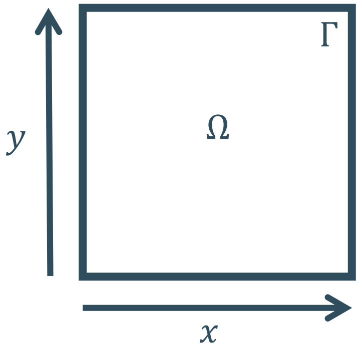
- Defining the problem, the domain of interest, and the initial and boundary conditions

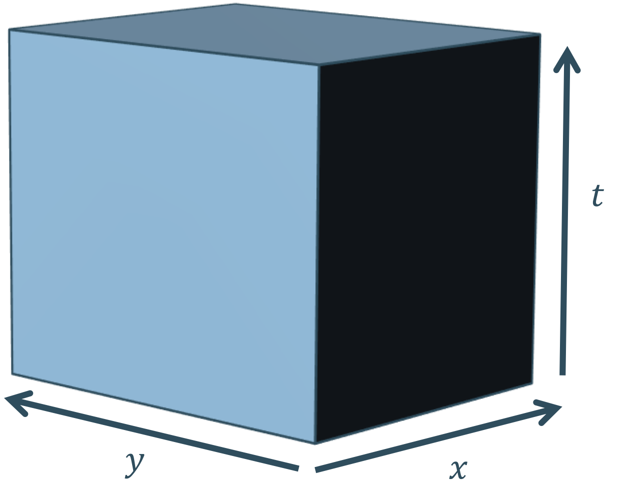
$$u(c) = \frac{\partial c}{\partial t} + \nabla.(-D\nabla c) - R(c) = 0$$

$$c = c(x, y, t), \qquad x, y \in \Omega, t \in [0, T]$$

$$c(x, y, 0) = c_{IC}, \qquad x, y \in \Omega$$

$$c(x, y, t) = c_{BC}\,, \qquad x, y \in \Gamma, t \in [0, T]$$





Training PINN Models

- Deriving the error for gradient descent

$$u(c) = \frac{\partial c}{\partial t} + \nabla.(-D\nabla c) - R(c) = 0$$

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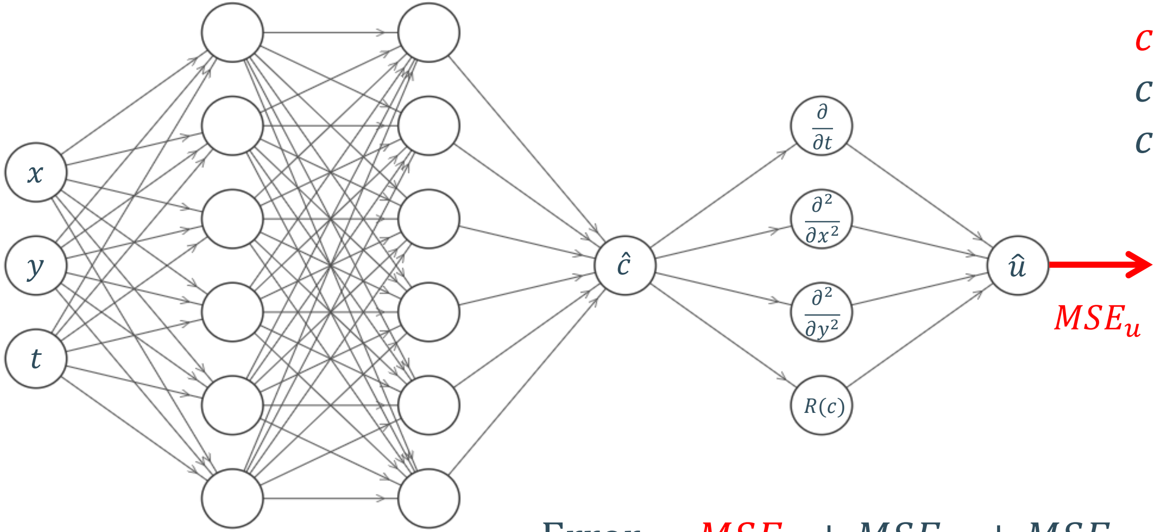
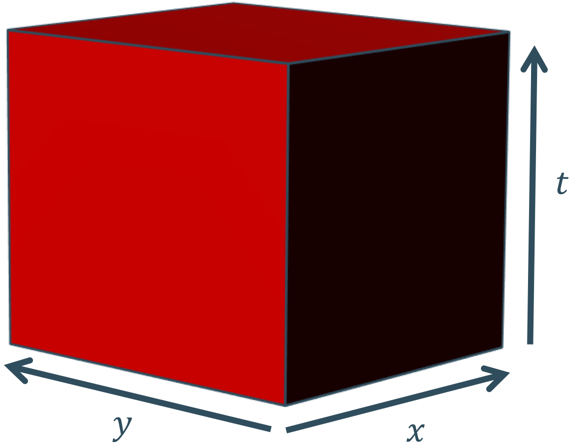


$$\text{Error} = MSE_u + MSE_{IC} + MSE_{BC}$$



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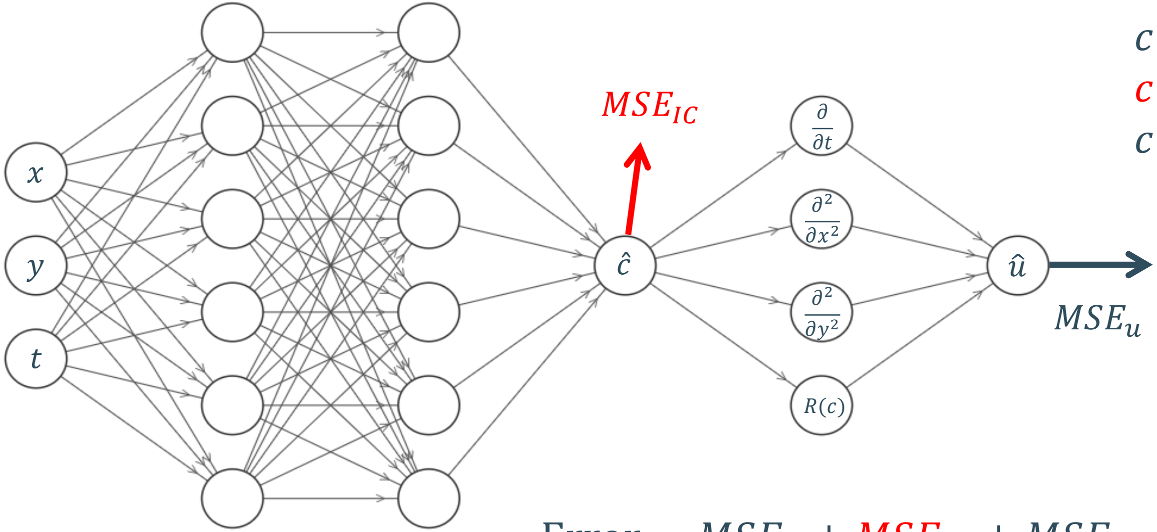

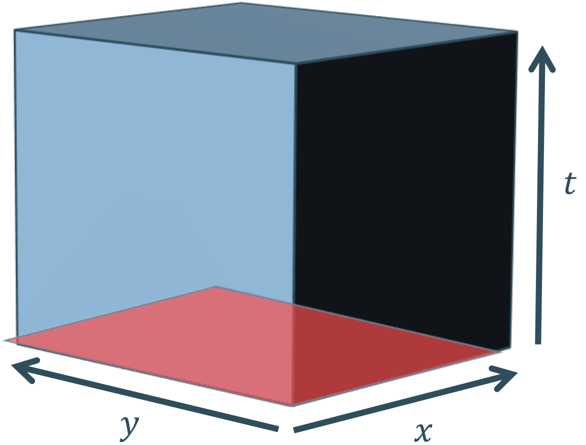

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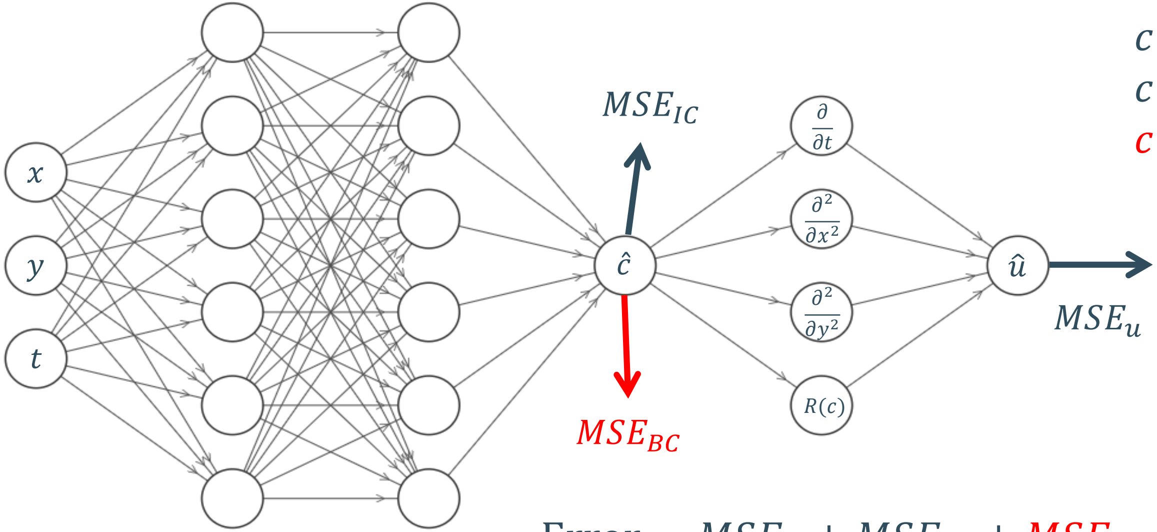

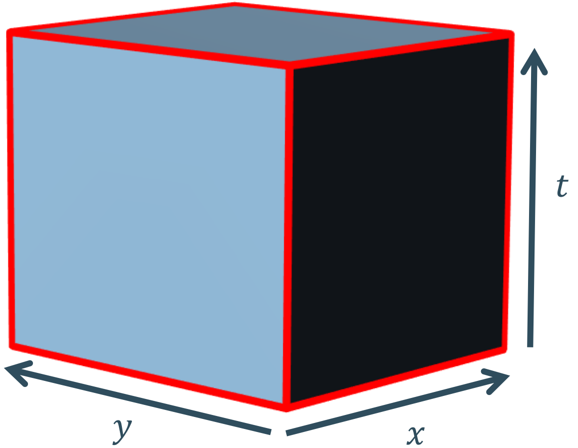

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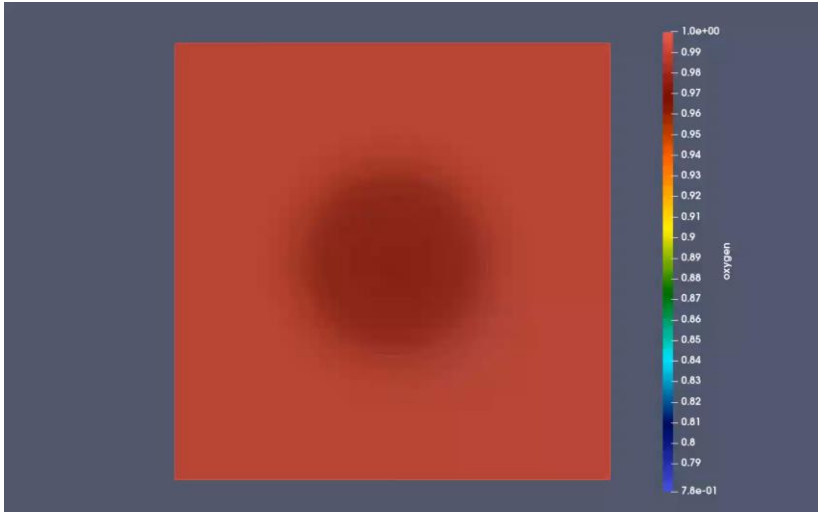
Implementing PINN Model

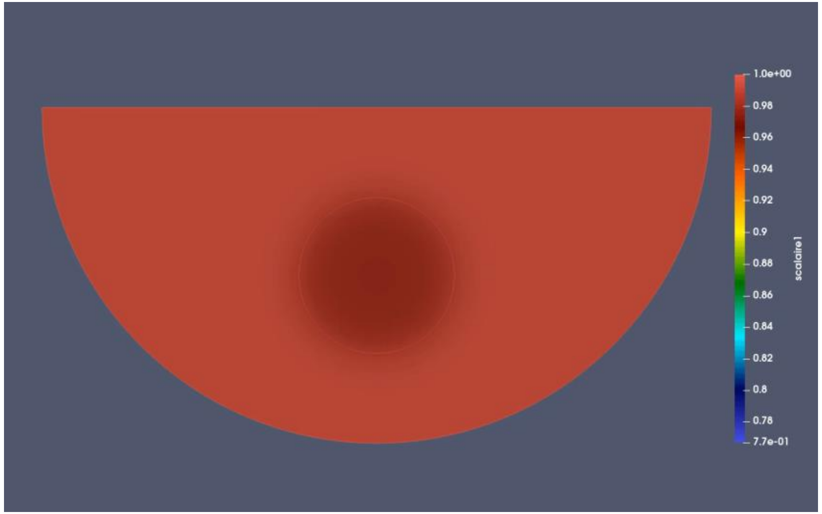
- Implemented using TensorFlow and NVIDIA SimNet
- Different diffusion rates for cells and culture environment
- Heaviside formulation to track variable diffusion and initial conditions
- Scaling and normalizing the problem is crucial
- Treating time becomes tricky for large time scales

Finite Element Results

- Oxygen concentration profiles showing consumption/supply



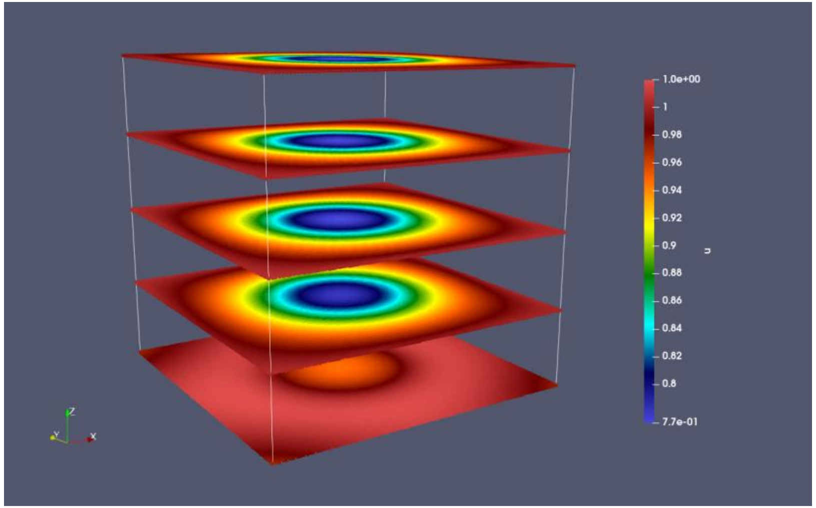
Rectangular well



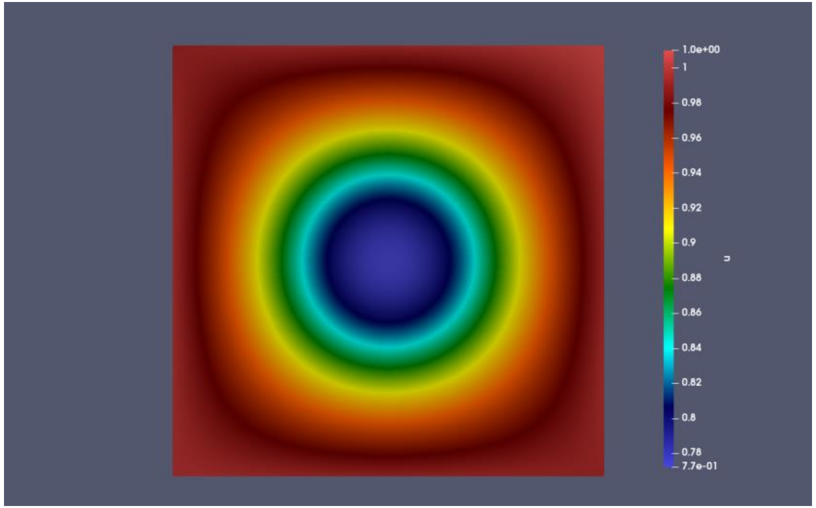
Circular well

PINN Results

- Oxygen concentration profiles showing consumption/supply

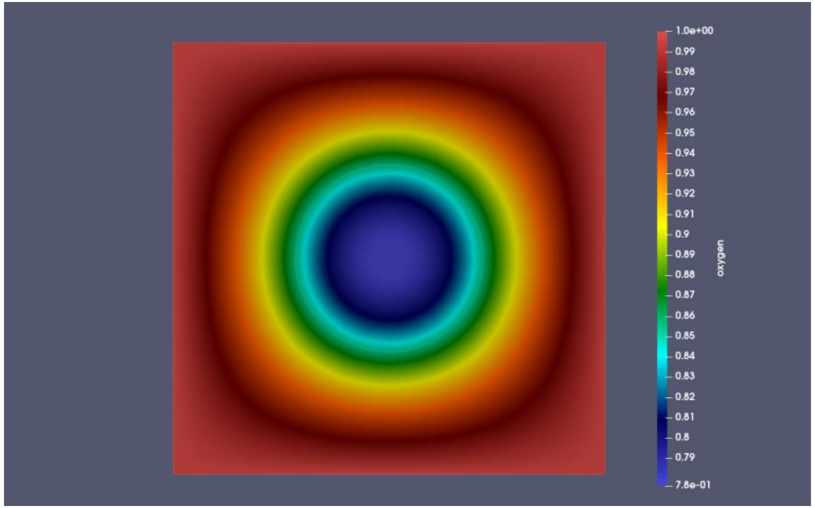


Time as the Z axis

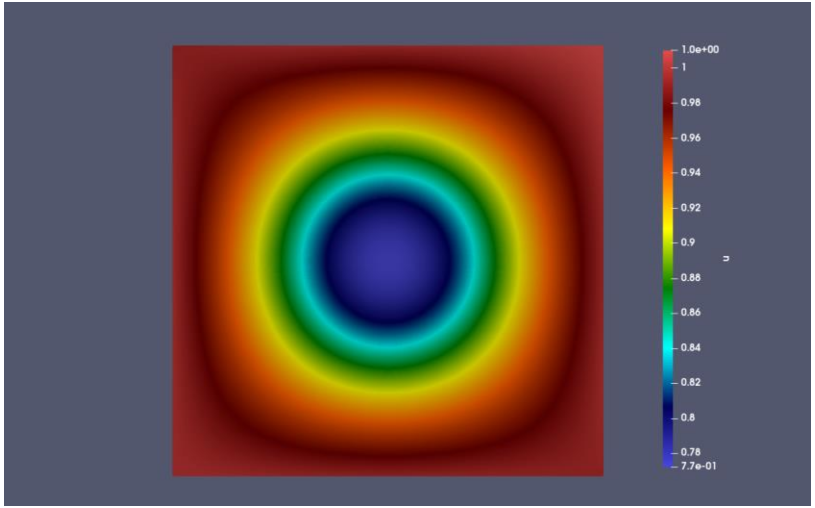


Final state

Numerical Simulation vs. PINN Solver

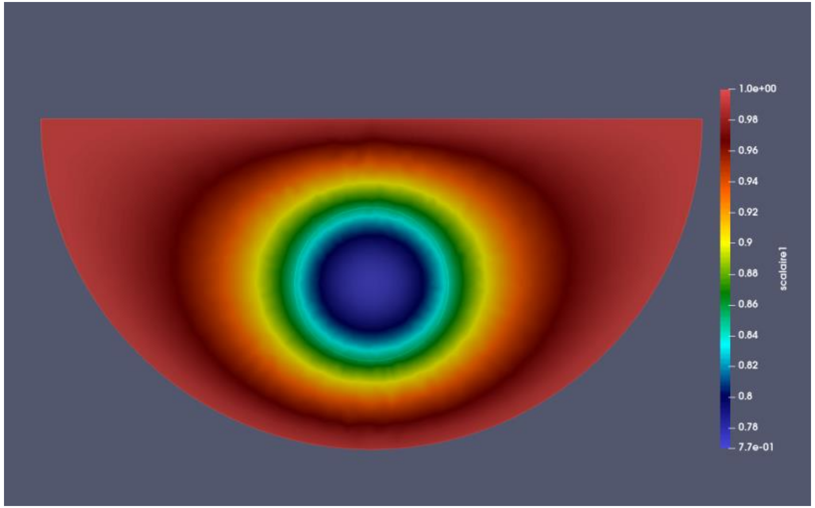


Final state using the
finite element solver



Final state using
the PINN solver

Numerical Simulation vs. PINN Solver



Final state using the
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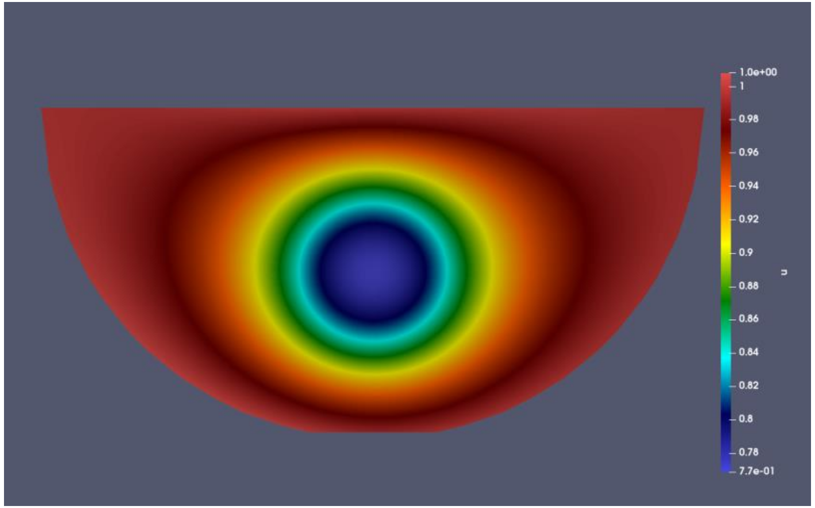

Final state using
the PINN solver

Conclusion

- Implanting pancreatic islets into microwells to increase viability
- Mathematical and computational modeling of the oxygen consumption and supply to assess cell viability and hypoxia
- Physics-informed neural networks (PINN) to solve governing equations
- Demonstrating the PINN model’s equivalence to the traditional numerical schemes in this case

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Thank you for your attention!

https://mbarzegary.github.io

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