Modeling Cell-Material Interactions in Wound Healing Scaffolds Using Machine Learning and Deep Learning Approaches

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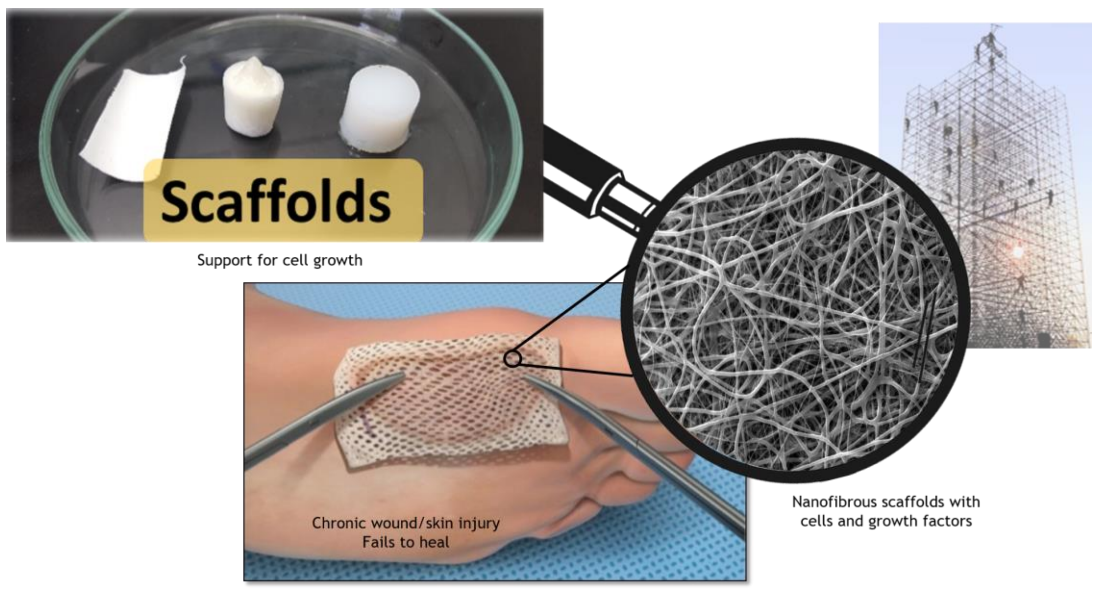
Introduction

1950s: Emergence of Artificial Intelligence (AI) as a field of study.

1980s–1990s: Growing interest in applying AI techniques across various **clinical settings in healthcare.**

2010s: Rapid expansion of AI-driven applications in **healthcare, revolutionizing diagnostics, treatment planning, and patient care.**

2010s–Present: Increasing use of AI and computational models to **optimize scaffold design** and **enhance tissue regeneration strategies.**



1970s: 1st generation of scaffolds – **Bioinert materials** introduced.

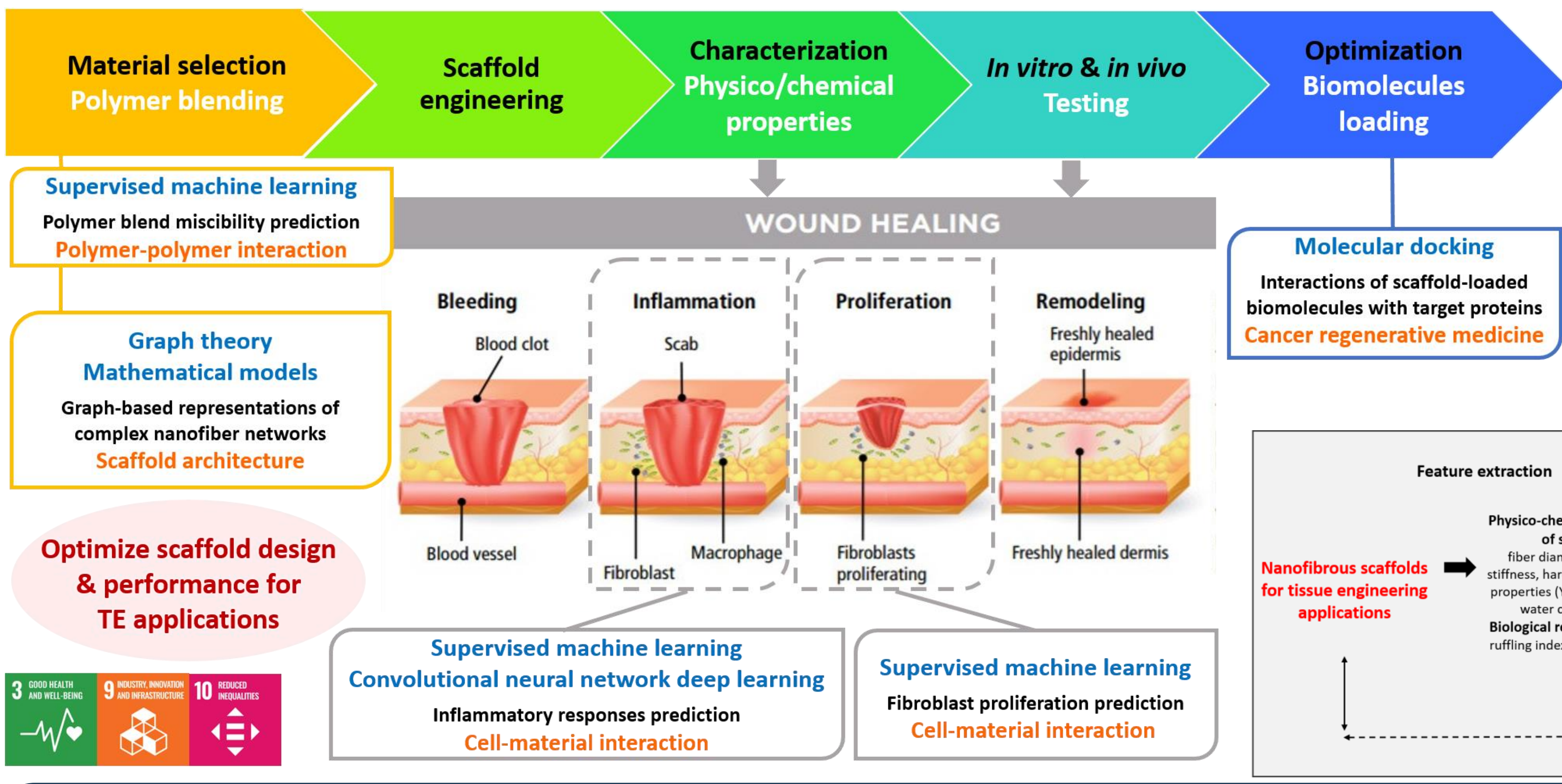
1980s: 2nd generation – Development of **degradable scaffolds.**

1990s: 3rd generation – Introduction of **bioactive scaffolds.**

2000s: 4th generation – Scaffolds capable of **encapsulating genes, cells, and molecules.**

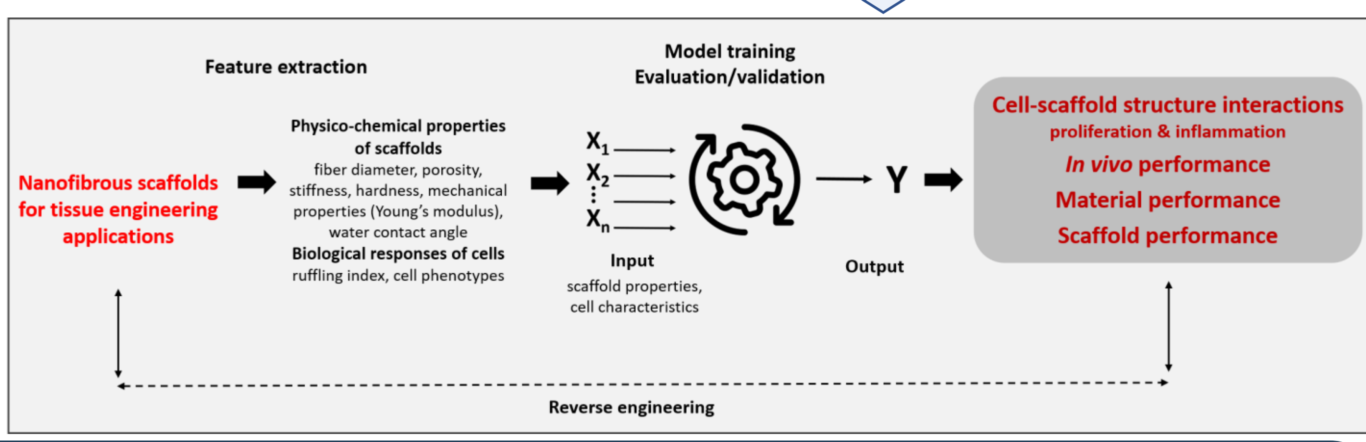
2010s: 5th generation – **Stimuli-responsive** scaffolds.

Significance of study: Reverse engineering of wound healing scaffolds via computational modeling



Today's challenges:

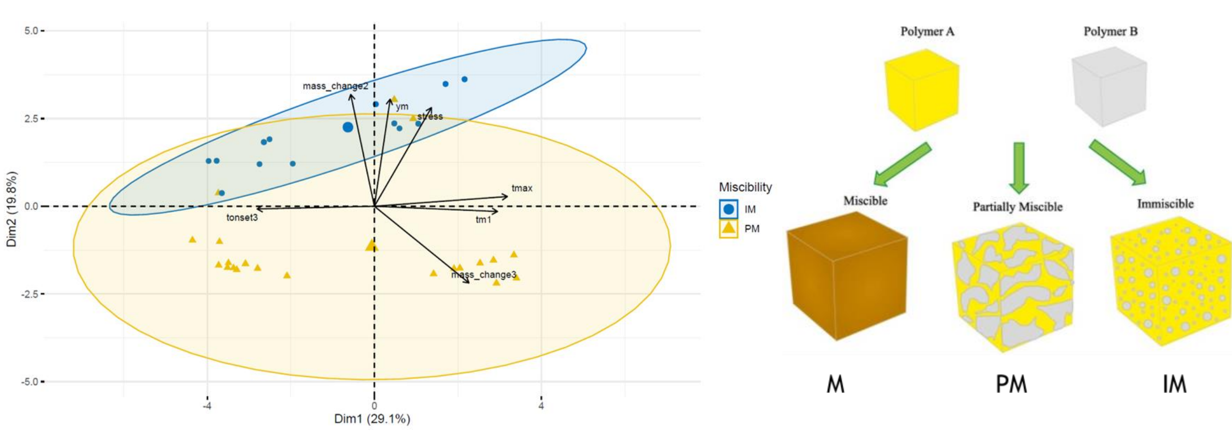
- In-depth understanding of **polymer-polymer and cell-material interactions** on scaffolds for tissue regeneration.
- Guide **scaffold design** and **improve performance.**
- **Sustainable and efficient research process.**



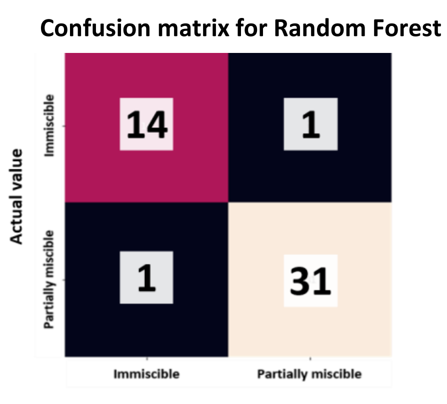
Results & Discussion

Predicting miscibility of polymer blends[1]

Miscibility: one of the key factors affecting the structure and properties of a polymer blend.



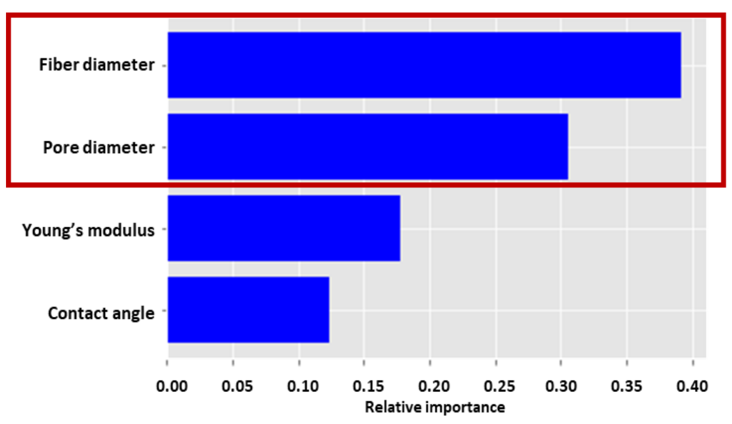
Two colored concentration ellipses IM and PM (size of ellipses determines by a 0.95 probability level). Principal component analysis (PCA) biplot for PC1 (29.1% explained variability) and PC2 (19.8% explained variability) of polyester/polysaccharides and polysaccharides/polyamides blends.



Model performance for Random Forest classifier

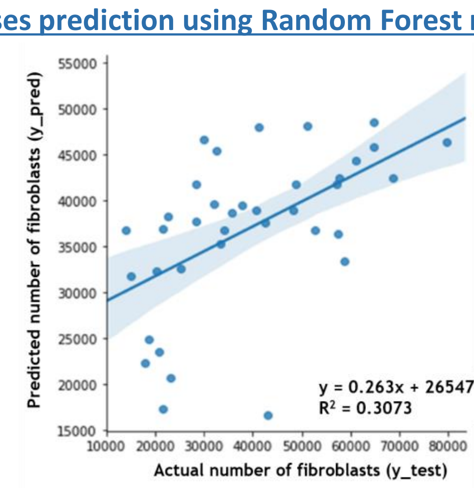
- Accuracy: 96.1% for the training set; 95.7% for the testing set.
- Testing set included 47 polymer blends.
- 14 out of 15 immiscible blends were predicted correctly.
- 31 out of 32 partially miscible blends were predicted correctly.

Predicting cell-material-interactions during the inflammation and proliferation phases[2]



Fiber diameter and **pore diameter** were identified as **key parameters** influencing *in vitro* cell proliferation and inflammatory responses.

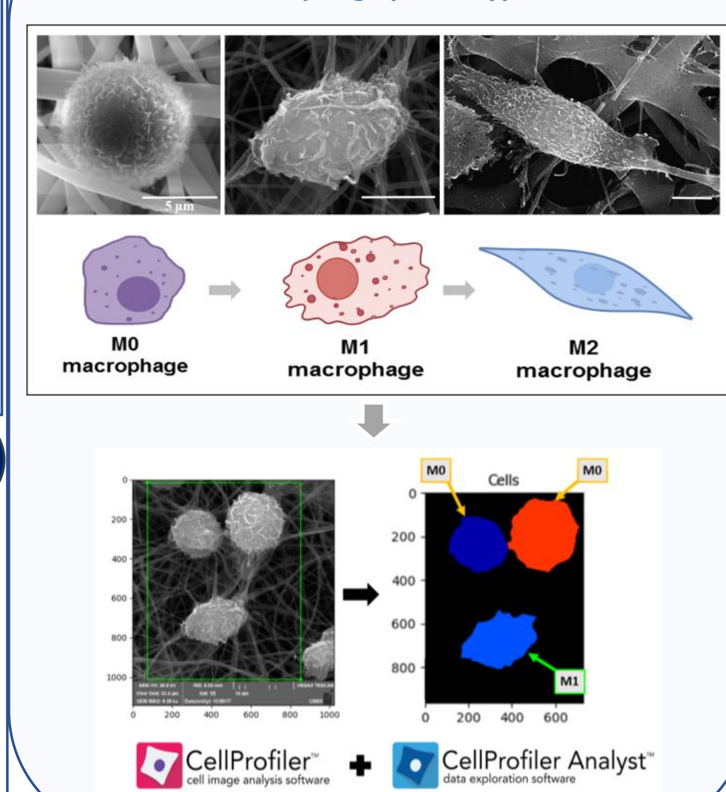
Cell responses prediction using Random Forest regression models

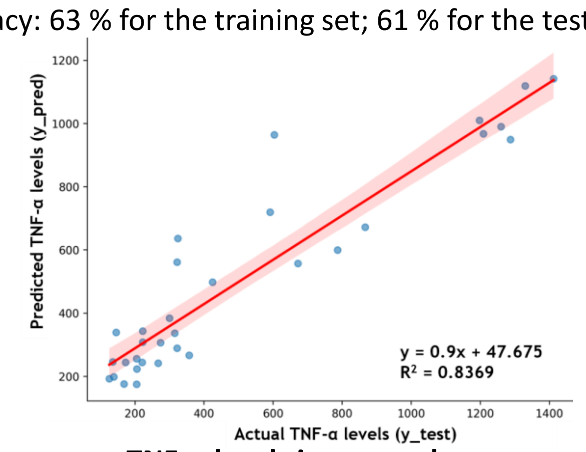


Fibroblast cell proliferation

Accuracy: 63 % for the training set; 61 % for the testing set.

CellProfiler and CellProfiler Analyst to classify macrophage phenotypes

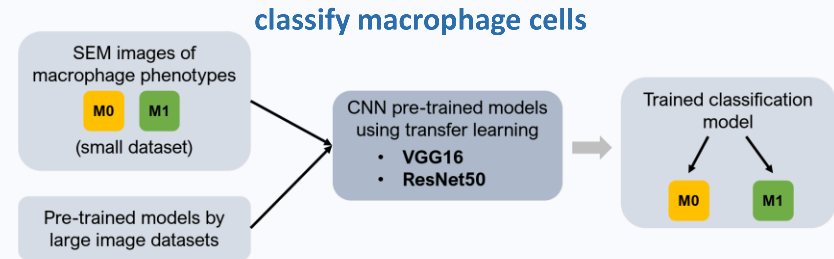




TNF-α levels in macrophages

Accuracy: 93 % for the training set; 89 % for the testing set.

Preliminary deep learning pre-trained modeling to classify macrophage cells



With 10 epochs, the VGG16 and ResNet50 models generated validation accuracies of 90.3% and 91.4% respectively.

Conclusion & Future Work

- **Polymer blends affect scaffold properties**, influencing **cell-material interactions.**
- **Fiber and pore diameters** are critical for **promoting cell growth and penetration in scaffolds. Predicting specific cell-scaffold interactions can enhance therapeutic outcomes.**
- **Future work:** investigating **graph theory** to **characterize complex nanofiber networks** and using **molecular docking** to study **interactions between scaffold-loaded biomolecules and target proteins.**

References
1. Sujeeun et al. (2020), *Royal Society Open Science*, *7*(12), 201293. doi.org/10.1098/rsos.201293
2. Sujeeun et al. (2023) Macromolecular Research, 31, 379–392. doi.org/10.1007/s13233-023-00155-4
3. Sujeeun et al. (2024, submitted)