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Technion Potential Contribution
to the
MAGNET Consortium
on
Development of technologies for engineering and 3D Bio-printing of cells, tissue and organs

11 April 2018

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Researcher	Affiliation
Prof. Shulamit Levenberg	Biomedical Engineering
Prof. Dror Seliktar	Biomedical Engineering
Prof. Gershon Elber	Computer Science
Prof. Anath Fischer	Mechanical Engineering
Prof. Nadav Amdursky	Chemistry
Prof. Oded Amir	Civil and Environmental Engineering
Prof. Nahum Rosenberg	Medicine

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Proposal for
Development of technologies for engineering and 3D Bio-printing of cells, tissues and organs

Shulamit Levenberg, Biomedical Engineering

Dean, Professor, Stanley and Sylvia Shirvan chair in cancer and life sciences

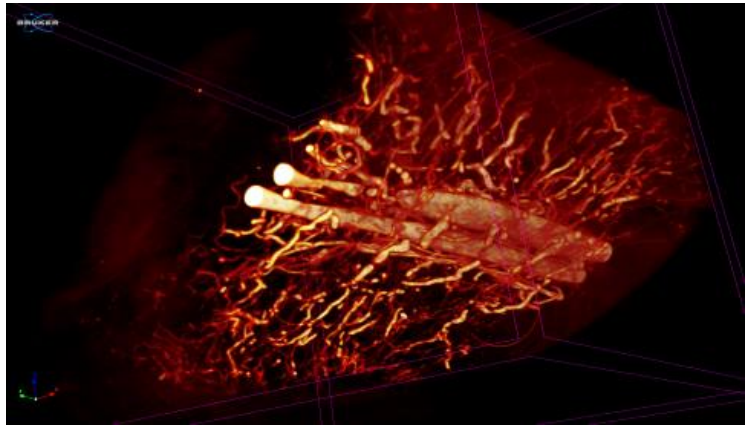
E-mail: shulamit@bm.technion.ac.il

Phone: 04-8294810

- Background of principal investigator -
  - Research Leader in Tissue Engineering
  - Former President of the Israel stem cell Society
- Relevant activity –
  - Interdisciplinary research on stem cells and tissue engineering.
  - Vascularization of engineered tissues.
  - 3D Bio-printing of engineered tissues for research (cardiac, blood vessels, pancreas).

The 3D-bioprinting center for printing cells and biomaterials at the Faculty of Biomedical Engineering, Technion

The 3D-bioprinting center offers printing paid-service according to user's application, as well as usage by trained users.



Sprouting from large vessels to create vascularized 3D bio-printed tissues

PCL printed matrix

The envisionTEC GmbH 3D-Bioplotter Manufacturer Series (https://envisiontec.com/3d-printers/3d-bioplotter/manufacturer-series/)

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Proposed Research Directions

- Structure and organization of 3D-printed tissues.
- Function of 3D-printed tissues.
- Biomaterials and growth media for 3D bio-printing.
- Cryopreservation.

Potential collaborations

- ❖Biomaterial companies
- ❖Cryopreservation companies
- ❖Cell therapy and cell expansion companies

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Proposal for
Development of technologies for engineering and 3D Bio-printing of cells, tissues and organs

Prof. Dror Seliktar, Biomedical Engineering Faculty

dror@bm.technion.ac.il; 04-829-4805

❖ Background of principal investigator -

- B.Sc. & M.Sc. In Mechanical Engineering (Drexel, Georgia Tech)
- Ph.D. in Biomedical Engineering (Georgia Tech)
- Post-doc in BioMaterials (ETH)

❖ Relevant activity –

- Hydrogel Biomaterials for Tissue Engineering and Cell Therapy
- Cell Culture Scaffolds and Bioink Development in 3D Printing
- Mechanobiology of Stem Cell Cultures in 3D

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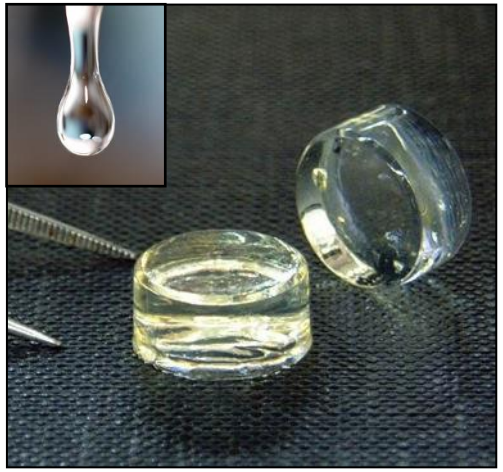
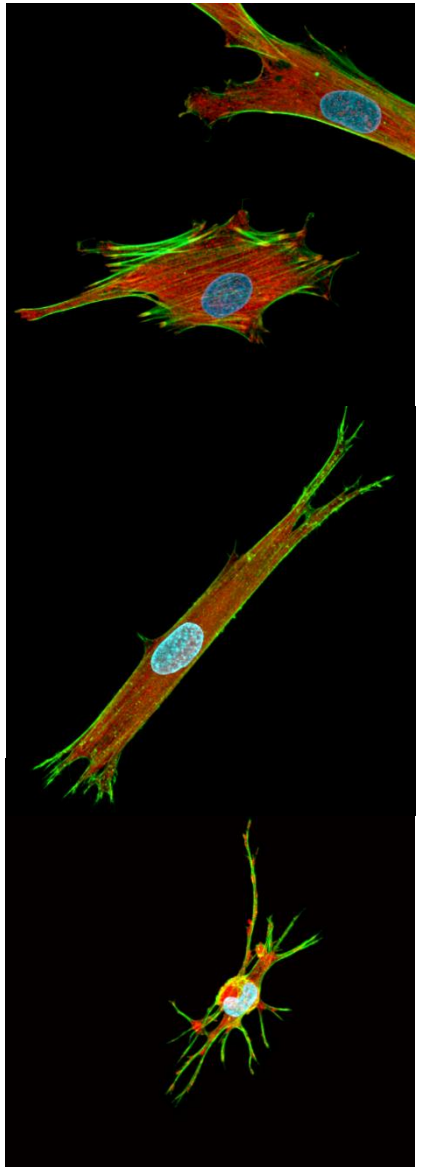
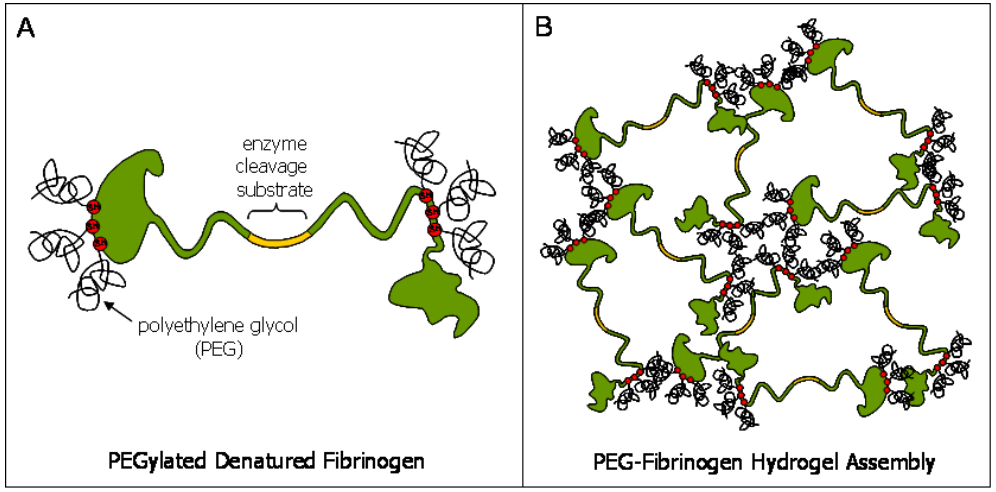
Semi-Synthetic Hydrogels as Bioinks

- Novel, highly biocompatible hydrogel technology developed in the Seliktar laboratory and licensed to **Regentis Biomaterials Ltd.**
- Used for traumatic injuries or diseased tissues (cardio, ortho, neuro).
- Currently CE-mark approved in the EU and awaiting FDA Approval (expected in 2020).







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Development of Cell Compatible Bioinks

- Hydrogel bioinks made from fibrinogen and synthetic polymers such as PEG and Pluronic
- Capable of chemical UV cross-linking
- Capable of physical temperature induced cross-linking (reverse thermal gelation)
- Highly biocompatible with cells and tissues
- Able to encapsulate cells during 3D printing and maintain viability and differentiation

Potential collaborations

❖ Industry/Academia working on 3D printers

❖ Industry/Academia working on tissue regeneration

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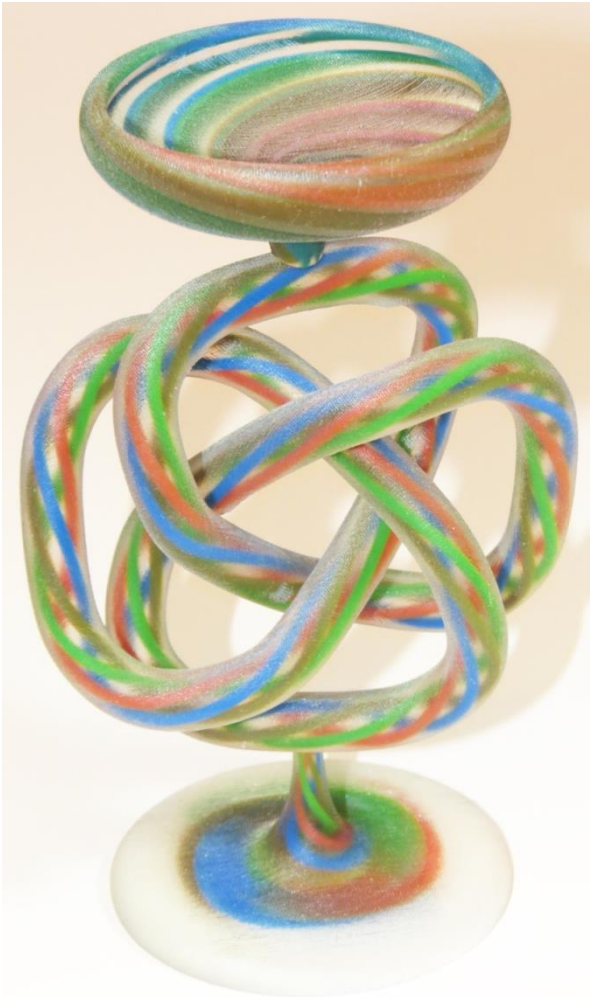
Prof. Gershon Elber, CS, Technion

gershon@cs.technion.ac.il, 0544-717-317

- Background of principal investigator -
  - Geometric Modeling
  - Computer Aided Design and Manufacturing
  - Design/analysis/manufacturing of free form **volumetric spline** models
- Relevant activity –
  - Multi level multiresolution **microstructures**' design in engineering
  - **Porous** geometry
  - **Heterogeneous** materials modeling:



3D heterogeneous material printing (courtesy of Stratasys Israel)

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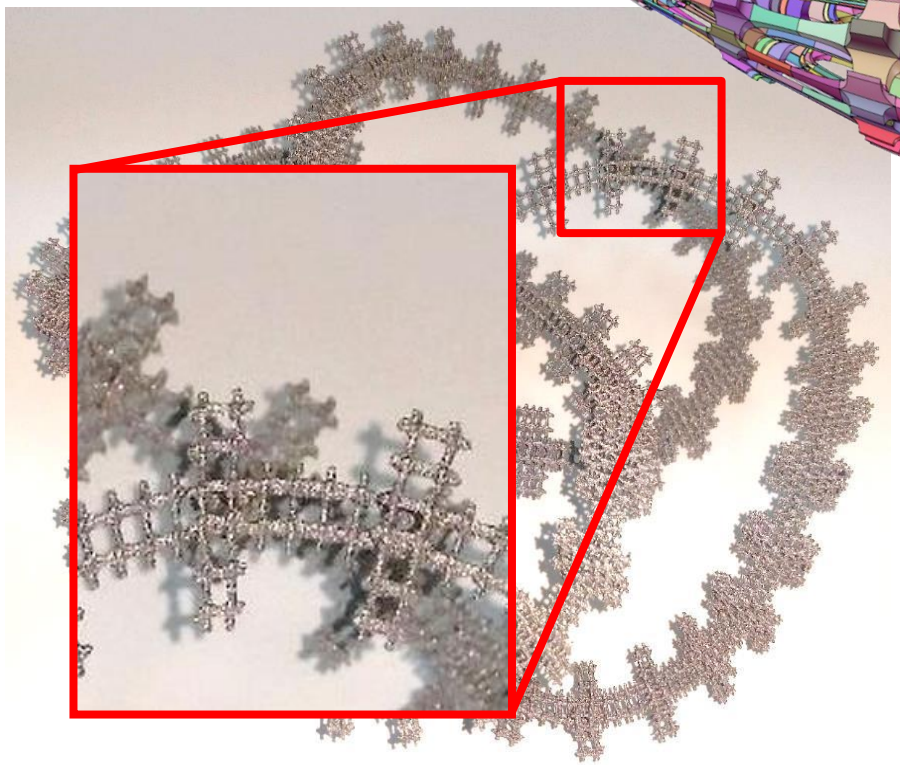
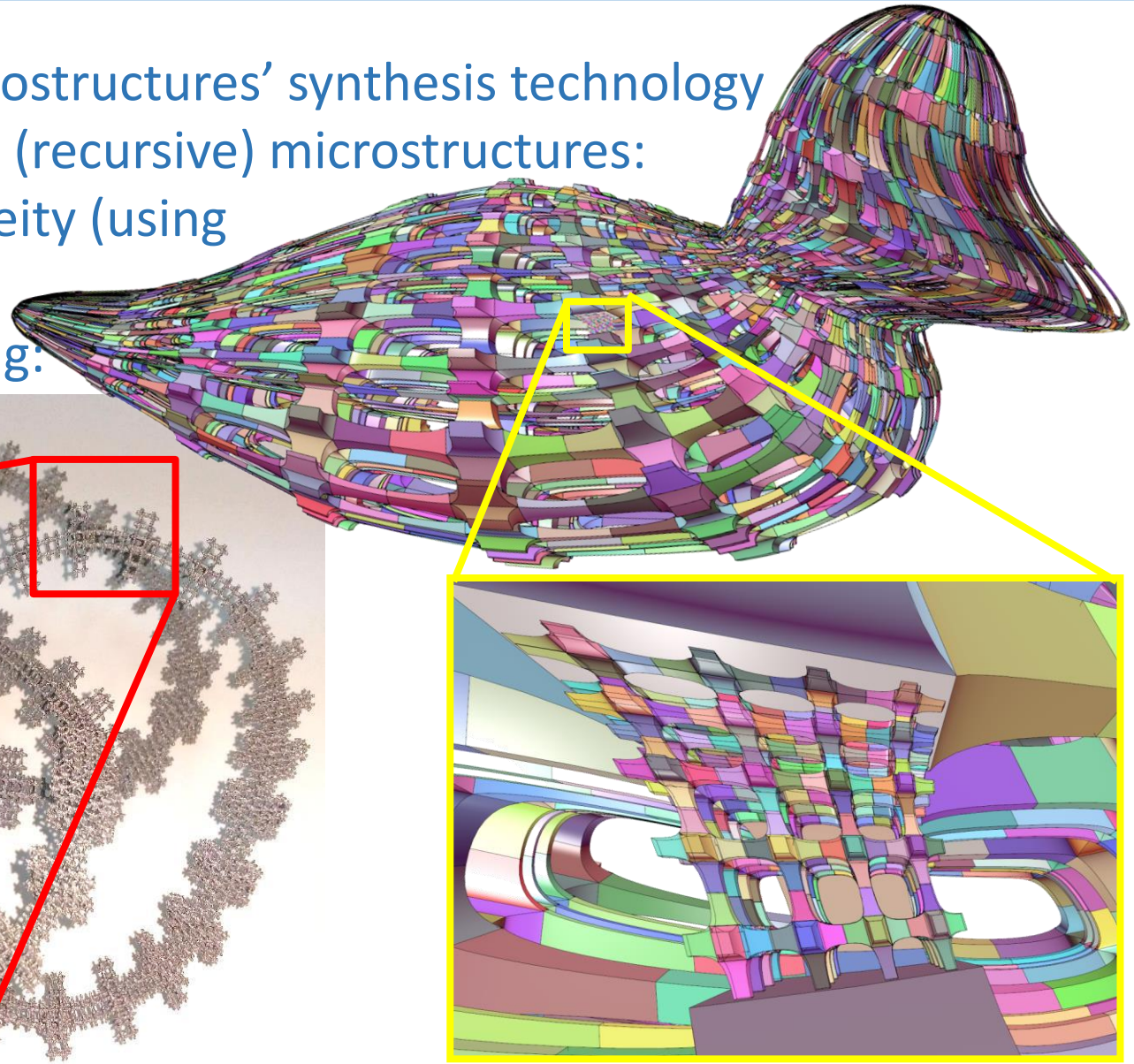
Designs and Manufacturing of Microstructure Scaffolds in bio(engineering)

- New & proven microstructures' synthesis technology
- Supports multilevel (recursive) microstructures:
- Handles heterogeneity (using trivariate splines)
- Supports 3D printing:





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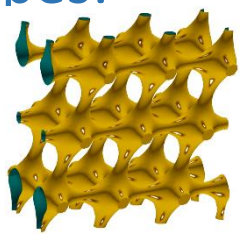
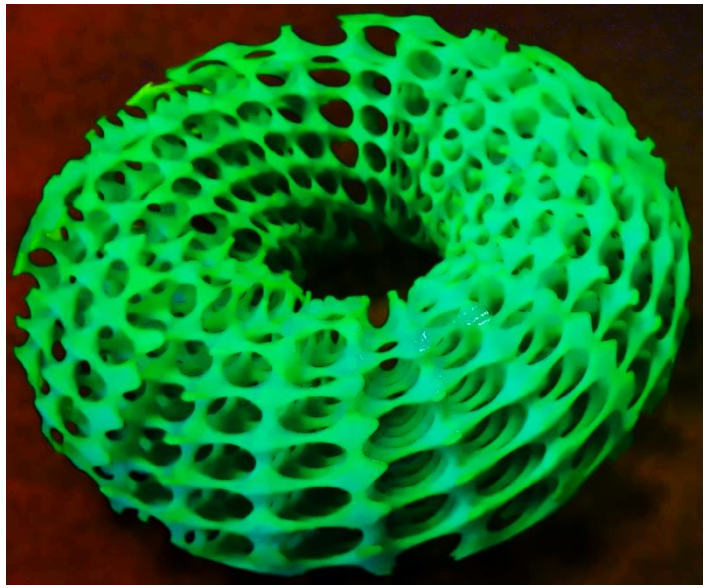
Proposed Research Directions

- Use of randomized heterogeneous multi-level microstructures toward design and manufacturing in biology & bioengineering
- Arbitrary global macro shapes:
- Arbitrary tile geometry:
- **Local control of individual tiles'** geometry/material properties





Potential collaborations

❖ Anyone wishes to exercise this new yet mature technology in biology or bioengineering:

- Gershon Elber. ``Precise Construction of Micro-structures and Porous Geometry via Functional Composition.'' The Proceedings of the 9th International Conference on Mathematical Methods for Curves and Surfaces (MMCS9), June 2016
- Ben Ezair and Gershon Elber. ``Fabricating Functionally Graded Material Objects Using Trimmed Trivariate Volumetric Representations.`` Proceedings of SMI'2017 Fabrication and Sculpting Event (FASE), Berkeley, CA, USA, June 2017

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Proposal for
Development of technologies for engineering and 3D Bio-printing of cells, tissues and organs

Anath Fischer, Mechanical Engineering, Technion

E-mail: meranath@technion.ac.il, Tel: 04-8293260

Background of principal investigator:

- Geometric Algorithms for 3D printing
- Design and analysis of bone porous micro-structures for 3D printing
- Modeling micro-scaffold-based implants for bone tissue engineering
- Topology optimization for bone tissue engineering

Relevant activity:

- Interdisciplinary research on design and analysis of bone porous scaffolds
- Algorithms for Multi-scale modeling and mechanical analysis of bone structures
- Topology optimization for bone scaffolds
- Learning algorithms for pattern classification and segmentation of bone micro-structures from SEM

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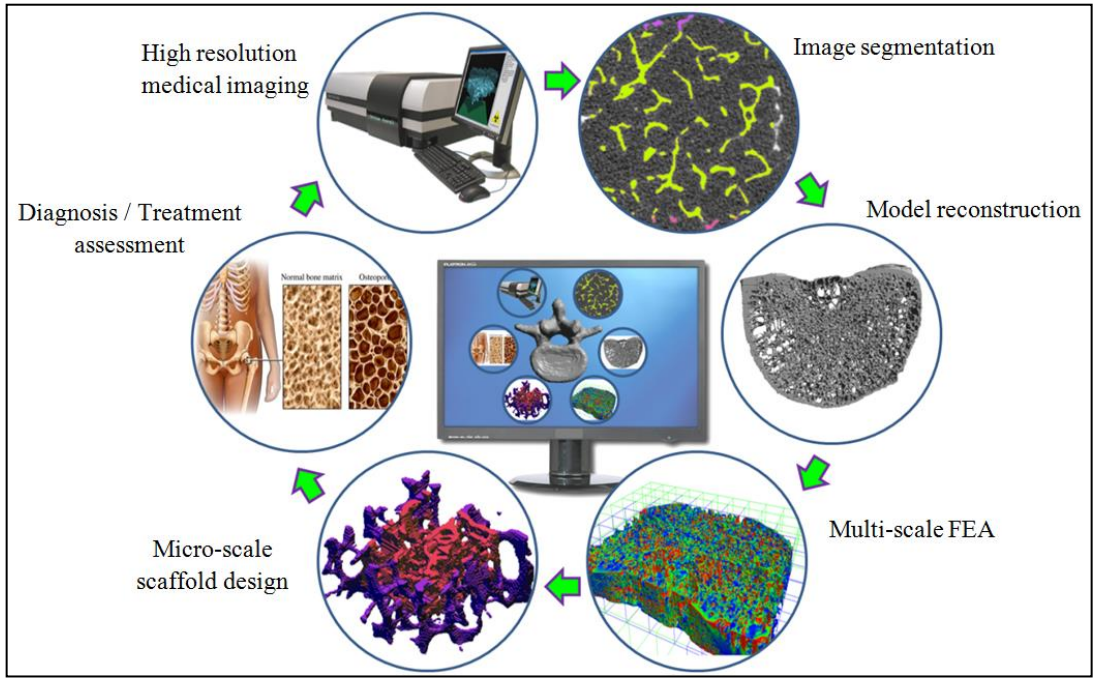
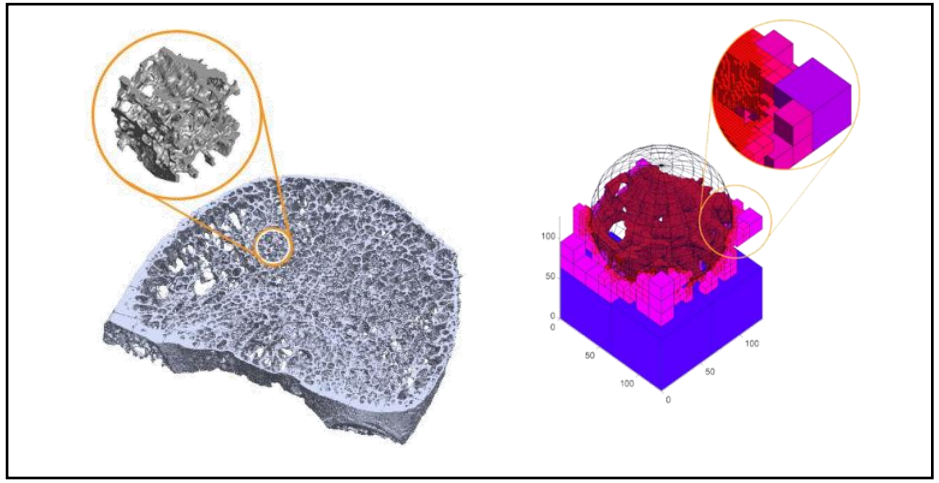
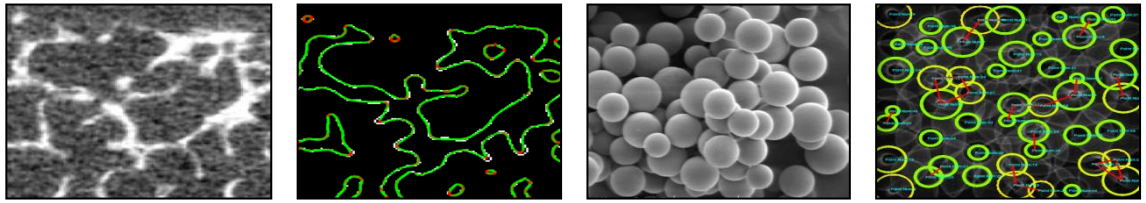
Computerized system for individualized diagnosis



Adaptive Multi-resolution Volumetric Geometric Modeling of Bone Micro-Structure

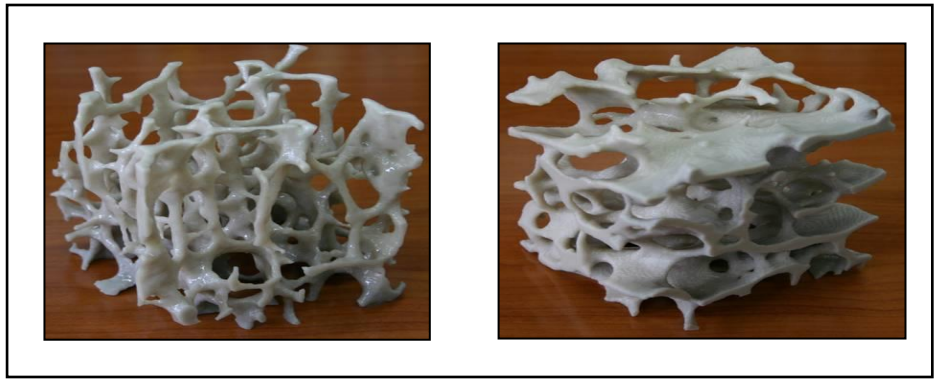


Geometric Analysis of Porous Structures based on Genetic Algorithms for 3D printing



3D printing models of bone micro-structures:

(a) specimen from lumbar spine; (b) specimen from femoral bone;



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Proposed Research Directions

- Multi-scale modeling of bone porous scaffolds
- Topology optimization (geometry and material) for bone scaffolds
- Design Mechanical analysis of degraded scaffolds
- Learning algorithm for visualization analysis of SEM images
- Learning methods for micro-structures pattern recognition

Potential collaborations

- Bio-printing companies
- Implant design companies
- Surgical and bio-mechanical robotics companies
- Companies that relate to rehabilitation

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Proposal for
Development of technologies for engineering and 3D Bio-printing of cells, tissues and organs

Prof. Nadav Amdursky, Schulich Faculty of Chemistry

E-mail: amdursky@technion.ac.il; Phone 04-8295953;

❖ Background of principal investigator -

- B.Sc in Biotechnology, Tel Aviv University (TAU)
- Ph.D in Biotechnology and Electrical Engineering (co-supervised by Profs. Ehud Gazit and Gil Rosenman), TAU
- 1st Post-doc in Materials and Interfaces, Weizmann (supervised by Prof. David Cahen)
- 2nd Post-doc in Materials and Bioengineering, Imperial College London (supervised by Prof. Molly Stevens)

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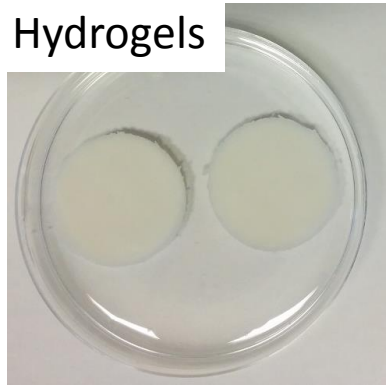
SUBJECT:

❖ Relevant activity –

- In my group we develop new type of materials, where we use proteins as our building blocks for the polymerization of the material. The materials that we form using only proteins with some chemical modifications of them can form a variety of different type of structures, with one common denominator: they are all not soluble in water and they are all free-standing.

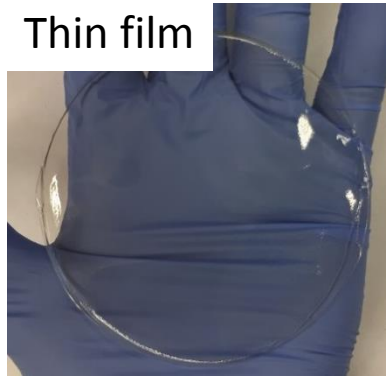
The type of materials that we can form without using sophisticated polymerization technique (such as electrospinning) are: hydrogels, gels (i.e., not containing water) and thin films.

Hydrogels



Gels

Thin film



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Proposed Research Directions

- We already showed that by using the hydrogels we can grow a beating patch of heart tissue on them.
- Another advantage of our protein-based materials is our ability to easily integrate important biological factors, such as growth factors, that are fundamental to any tissue growth.
- In my group we further study how we can make these structures to be electrically conducting, while focusing on different charge carriers, electrons or protons/ions. The ability to make them conductive can be attractive mainly for heart tissues.

-Potential collaborations

❖Since our starting material is low cost, we can make a lot of it. In our next step we would like to test the ability to **3D bio-print our material** for its further use as a scaffold for the formation of complex tissues and even organs.

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Development of technologies for engineering and 3D Bio-printing of cells, tissues and organs

Asst. Prof. Oded Amir, Civil & Environmental Engineering

odedamir@technion.ac.il, 04-8293041

❖ Background of principal investigator -

- Head of Structural Optimization Research Group, Technion

-Expertise in structural optimization, particularly topology optimization

❖ Relevant activity –

-Member of AATiD (MAGNET consortium) on Titanium 3-D printing of load-bearing components for the aviation industry

-10 years of research experience in topology optimization, in particular large-scale 3-D design using high performance computing

-Expert knowledge in topology optimization with nonlinear materials: hyperelastic, elasto-plastic, elastic-damage, etc.

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SUBJECT: Structural Topology Optimization

- The research group, headed by Prof. Oded Amir, focuses on the formulation, development and application of **advanced computational methods for the optimal design of structures**, in particular using three-dimensional topology optimization
- Topology optimization is a **generic approach** for finding optimal distribution of material in a given design space. The approach is widely applied in the aerospace and automotive industries, alongside 3-D printing, which makes it possible to produce structural configurations with complex geometry
- The group has **extensive experience in the context of 3-D printing** (in the framework of the "AATiD" consortium); in optimal design with hyperelastic and elastoplastic materials; and in the development of computational methods using high performance computing (HPC)
- More info in the group's website: www.structopt.net.technion.ac.il

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Proposed Research Directions

- Design of **biological metamaterials** with desired physical and biological properties, using computational methods of topology optimization (popularly known as generative design, morphogenesis)
- **Design of tissues, implants and artificial organs** using computational optimization methods, to achieve desired behavior while taking into account the integration into the surrounding tissue
- Consideration of **manufacturing constraints** of biomedical 3-D printing in formulating optimal design problems and in their computational implementation

- Potential collaborations

❖Bio-medical researchers and engineers that seek computational design methods for finding non-intuitive design solutions – from the micro (material) scale to the macro (e.g. implant) scale

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Nahum Rosenberg MD, FRCS, FACULTY OF MEDICINE

nahumrosenberg@hotmail.com; Phone 054 4685130

❖ Background of principal investigator -

- Orthopedic Surgeon
- Research – human osteoblast mechanical stimulation
-

❖ Relevant activity –

- Experimental setup for mechanical stimulation of human osteoblasts in vitro
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SUBJECT: Bone regeneration

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Mechanical stimulation of osteoblasts in vitro

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Proposed Research Directions

- Expansion of human osteoblasts in vitro by mechanical stimulation

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Potential collaborations

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For further information please contact us:

Technion R&D Foundation Ltd.

- Benjamin Soffer
  - Tel: 04-8294851
  - Mobile: 052-3331276
  - e-mails: sofferb@trdf.technion.ac.il

- Boris Herscovici
  - Tel: 04-8293137
  - Mobile: 052-8447786
  - e-mails: borish@trdf.technion.ac.il

- Lior Harpaz
  - Tel: 04-8295966
  - Mobile: 054-9900102
  - e-mails: liorh@trdf.technion.ac.il