Dekel Rosenfeld, PhD
Department of Biomedical Engineering
Tel Aviv University, Tel Aviv, Israel
Email: dekelr@tauex.tau.ac.il

Zimin Institute for Engineering Solutions Advancing Better Lives

Title: Magnetic System for Remote Control on Cortisol Release from Bioelectronic Implants

Principal Investigator: Dekel Rosenfeld, PhD
Senior Lecturer
Biomedical Engineering, Faculty of Engineering
Tel Aviv University

Scope of Research: Medical equipment/Medical and behaving sensing

Dekel Rosenfeld, PhD
Department of Biomedical Engineering
Tel Aviv University, Tel Aviv, Israel
Email: dekelr@tauex.tau.ac.il

ABSTRACT (250 words)

The adrenal glands produce different types of hormones, including the stress hormones cortisol and (nor)epinephrine. Imbalance of stress hormones is associated with mental health disorders and currently controlled via drugs, which suffer from limited temporal precision and accompanying side effects due to systemic delivery. The field of bioelectronic medicine aims to develop methods to stimulate electrogenic cells within organs for activation of biological mechanisms and to treat diseases[1]. Combining the recent achievements of this emerging field with cell therapy approaches offer alternative for stimulation of organs with poor function, with on demand control on transplanted cells.

This project will focus on developing bioelectronic implants transplanted with hormones producing cells. Magnetic nanocomposites will be generated with hydrogel embedded with magnetic nanoparticles (MNPs) which dissipate heat upon exposure to alternating magnetic fields (AMFs) with high frequencies and low amplitudes (~10s mT). A small size magnetic coil device will be designed to produce AMFs, for remote control on cells seeded within the implant. Feasibility of the system will be demonstrated by triggering cortisol release from adrenal cells which express the heat sensitive calcium-permeable ion channel TRPV1 with a temperature threshold of 43 ^{o}C, allowing calcium-dependent hormone release.

This project will pave the way to stimulation of cells which bear thermally sensitive ion channels and will pioneer the combination of cell therapy with bioelectronic medicine approaches. Moreover, the demonstration of on demand secretion of cortisol will open new avenues for the treatment of mental health disorders and in understanding the involvement of stress hormones in neurological diseases.

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INTRODUCTION

Hormonal imbalance, including low or high levels of hormones in the bloodstream, is a consequence of various health disorders and dysfunction of endocrine organs. The offered treatments include administration of exogenous hormones, which suffer from side effects and lack in measureable variables to estimate the quality of the treatment. Therefore, there is a growing demand for novel therapeutic alternatives to avoid drugs treatment and to allow on demand hormone release. Both basic and applicative research will benefit from new approaches for on demand hormone release and for better understanding the involvement of hormones in biological pathways.

The adrenal gland is an endocrine organ responsible for secretion of hormones, influencing health conditions including mental health disorders[2]. 1 out of 5 adults in the US are likely to develop a mental disorder, resulting in the highest burden on the US economy[3,4]. Adrenal stress hormones, (nor)epinpherine and cortisol (or corticosterone in rodents), are imbalanced in mental health disorders, demonstrating both low and high levels. Inconsistent cortisol levels were associated with depression[5, 6], whereas low cortisol levels were identified in Post Trauma Stress Disorder (PTSD)[7]. Moreover, it was demonstrated that exogenous cortisol administration can influence PTSD-memory formations[8]. Release of cortisol, is a calcium dependent process, and can be triggered through ion channels on the cell membrane[9].

I have pioneered a new approach to trigger the release of cortisol using a magnetothermal approach, mediated through activation of the transient receptor potential vanilloid family member 1 (TRPV1)[10]. TRPV1 is a non-selective cation channel that is calcium-permeable and can be activated by capsaicin, heat > 43 ^{o}C and pH < 5.9[11 12]. The method relies on magnetic nanoparticles (MNPs) of iron oxide Fe_3O_4 in a size of 20-22 nm which demonstrate hysteretic heating when exposed to alternating magnetic fields (AMFs) with high frequency (100-600KHz) and low amplitudes (10-60 mT), thus reaching efficiently the temperature threshold of TRPV1 (**Fig. 1a**). Translating this approach to

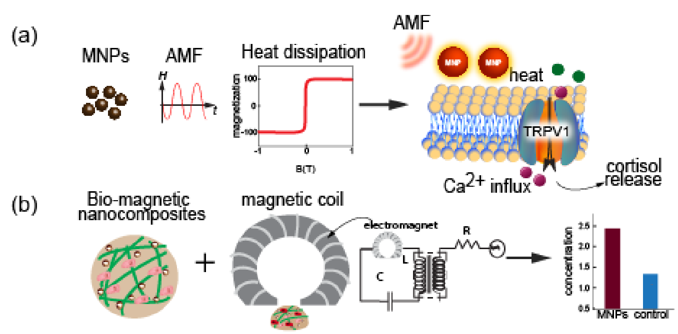

Figure 1: *(a) MNPs dissipate heat when exposed to AMF. Adrenal cells express heat sensitive ion channel that can trigger Ca^{2+}-dependent cortisol release (b) proposed approach for translating the magnetothermal cortisol release to bio-magnetic nanocomposites and the magnetic coil design*

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transplanted cells will allow on demand control on hormone release in cases of organ failure and opens new avenues in triggering other types of cells that express similar heat sensitive ion channels.

SPECIFIC AIMS

This research aims to develop a magnetic system for modulating cells within bioelectronic implants. Bio-magnetic nanocomposites will be synthesized using functionalized MNPs embedded in hydrogel. Then, a small size portable magnetic coil device generating high frequency AMFs (100-500 KHZ) with low field amplitudes (~10-60 mT) will be developed for magnetic stimulation of the implants. Finally, the implants will be used to demonstrate on demand release of cortisol from the embedded cells (**Fig. 1b**).

Aim 1: Develop and optimize bioelectronic implants comprised of bio-magnetic nanocomposites seeded with cortisol secreting adrenal cells

Aim 2: Design a magnetic coil that can stimulate cells within bioelectronic implants with AMFs of high frequency and low amplitude

Aim 3: Utilize the magnetic coil system to demonstrate on demand cortisol release from bio-magnetic nanocomposites

METHODS

Aim 1-Develop and optimize bioelectronic implants comprised of bio-magnetic nanocomposites seeded with cortisol secreting adrenal cells: For fabrication of the magnetic nanocomposites, surface functionalized MNPs will be embedded within hydrogel. The hydrogel will serve as a support matrix for hosting the MNPs and providing a three-dimensional (3D) environment for cell growth, maintaining metabolic activity of the cells. The heat dissipated by the MNPs within the hydrogel under AMF stimulation, will be accounted for and optimized using electron microscopy examination and thermogravimetric analysis. For MNPs synthesis we will first prepare an iron-oleate complex by heating to reflux (60 °C) sodium oleate and $FeCl_3 \cdot 6H_20$ for one hour under N_2 followed by overnight drying. We will then prepare magnetite nanoparticles from that mixtures by degassing the iron-oleate mixture at 90 °C for 1 h with a combination of 2:1 (volume ratio) of 1-octadecence and dibenzyl ether. The mixture will be heated to 200 °C under N_2, followed by two washes in chloroform. For making the MNPs hydrophilic and biocompatible, the hydrophobic layer on the surface of the MNP will be functionalized using intercalation of amphiphilic polymer (PMAO) grafted with poly ethylene glycol (PEG). MNPs will be sonicated together with the PMAO-PEG grafted polymers dissolved in chloroform for 1 hour followed by

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chloroform evaporation overnight. MNPs will then be sonicated with buffer followed by two washes with distilled water.

Adrenal cell culture will be generated from primary adrenal cells that will be kept in physiological conditions to preserve metabolic activity. The adrenal gland will be extracted from the animal and the cortex layer will be separated from the adrenal medulla. Using collagenase the adrenals will be mechanically disturbed and cells will be filtered to prevent tissue residues in the culture.

For creating fibrin hydrogels, MNPs will be mixed with fibrinogen, cells will be mixed with throbmin and after mixing those two solutions together they will be placed in inserts and polymerized at 37 ^{0}C. Growth medium will be added to the plates. Cells viability will be examined using Alamarblue metabolic assay. Moreover, we will use vibrating sample magnetometer to examine the magnetic properties and hysteresis heat dissipation of the magnetic hydrogels.

Aim 2-Design a magnetic coil that can stimulate cells within bioelectronic implants with AMF of high frequency and low amplitude: A gapped toroidal electromagnet which assumes a uniform magnetic flux in the gap of the toroid will be designed (gap width~8-10 mm). The gap will be designed such that the hydrogel (total diameter 5-6 mm) can be placed below the coil and at the gap opening, to experience AMF stimulation. Such design will be suitable for future in vivo applications where the coil is held above the skin of the hydrogel implantation site (**Fig. 1b**). A parallel resonance RLC circuit drives the current in the wires wrapping the toroidal electromagnet[13]. A cooling system will be added around the coil using tubes that are constantly flowing cooled water to eliminate additional heating from the coil. For operating the coil we will use a function generator to create a sine wave and the system will be tuned to reach a resonance frequency. We will then be able to define the desired amplitude that matches the magnetic properties of the MNPs. Using IR camera, calorimetry measurement of the heating efficiency of the MNPs within the hydrogel will be performed and total temperature increase of the construct will be examined. By placing the hydrogel within inserts thermally isolated from the environment, we will use temperature probe (optical fiber) to estimate the amount of heat released by the hydrogel to the medium (expecting negligible heating with most heating preserved locally within the hydrogel). The initial parameters for the coil circuit will be 150 KHz with field amplitude of 30-40 kA/m, which were proven efficient in previous experiments with 20-22 nm iron oxide MNPs [14]. In case we will observe different magnetization behavior of the magnetic composites, we will adjust the circuit parameters

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accordingly. Heating efficiency is termed Specific loss power (SLP), calculated by: SLP= $\frac{Cp}{m}\frac{\Delta T}{\Delta t}$ with ~800 $W/g_{[Fe]}$ in our previous observations. (Cp=specific heat capacity of water, m=concertation, $\frac{\Delta T}{\Delta t}$ = rate of temperature change)

Aim 3-Utilize the magnetic coil system to demonstrate on demand cortisol release from bio-magnetic nanocomposites: For keeping the metabolic activity of adrenal cells, the magnetic bio-hybrid embedded with cells will be grown inside a metabolic shaker under conditions of 95% Oxygen/5% CO_2 and 37 ^oC. We will grow the bio-magnetic implants for up to 5 days (based on our preliminary results, **Fig. 2d**) under AMF stimulation. AMF stimulation will be performed at repeating stimulation points daily during the 5 days growth period. We will compare the hormone levels in three groups: (1) cells grown within magnetic hydrogel with AMF stimulation, (2) cells grown within the magnetic hydrogel without AMF stimulation and (3) cells grown within hydrogel without MNPs and with AMF stimulation. We will compare several stimulation paradigms: (1) ramping the temperature to 43 ^oC five times daily for 5 days, (2) ramping the temperature to 43 ^oC for five times only at day 1, and (3) ramping the temperature to 43 ^oC for five times only at day 5. To estimate the hormone release from the cells to the medium, medium will be collected at the end point of every experiment and will be processed to detect corticosterone levels using ELISA. Moreover, immunohistochemistry staining post-stimulation will be performed to verify cell activation using the neural activity marker c-Fos. Cells will be fixated within the hydrogels using 4% paraformaldehyde (PFA) for 15 minutes followed by three washes with PBS. Cells will be permeabilized with 0.3% (vol/vol) Triton X-100 and blocked with 5% serum in PBS. We will then incubate the hydrogels with a solution of primary antibodies followed by incubation with secondary antibodies, with dual staining of c-Fos and TRPV1.

PRELIMINARY RESULTS

I created a magnetic gel embedded with MNPs. The magnetic gel demonstrate heat dissipation when exposed to AMF with frequency of 15 KHz and field amplitude of 35 kA/m, with ability to fast increase and decrease the gel temperature with repeated cycles of ON/OFF AMF stimulation (**Fig. 2a,b**). Moreover,

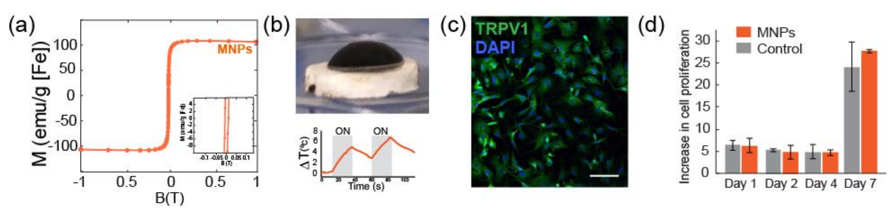

Figure 2: *(a) magnetization curve of synthesized and functionalized MNPs demonstrating high magnetization saturation, suggesting efficient heat dissipation (b) magnetic nanocomposite of hydrogel embedded with MNPs. Under AMF the entire gel is heated by the MNPs as measured with infer-red camera. (c) Primary adrenal cell culture demonstrating expression of the heat sensitive ion channel TRPV1. Scale bar= 40 µm (d) Adrenal cells viability and proliferation rate (Alamarblue assay) with and w/o the presence of MNPs suggesting high viability and confluency reached at day 7.*

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we were able to create primary adrenal cell culture from adrenal glands of adult rat, demonstrating expression of the ion channel TRPV1 in about 30% of the cells in culture. Adrenal cells demonstrated high viability even when incubated with MNPs in the culture, and the proliferating cells achieved confluency on day 7, with and without the presence of the MNPs (**Fig. 2c,d**).

I have demonstrated that cortisol release can be controlled on demand from adrenal glands of rats when activating TRPV1 ion channel, mediated by MNPs heat dissipation under AMF stimulation (**Fig. 3a,b**). Moreover, post stimulation we identified c-Fos expression in the adrenal cells suggesting cell activation under the AMF stimulation (**Fig. 3c,d**). Importantly, our preliminary findings indicate TRPV1 as dominant contributor to the magnetothermal effect, demonstrated by blocking the response with TRPV1 antagonist[10].

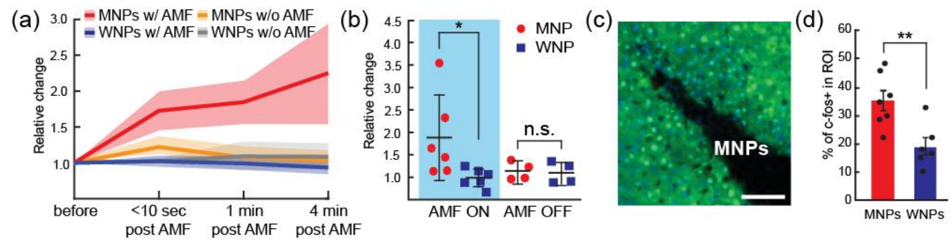

Figure 3: (a) cortisol level post-AMF stimulation of adrenal glands injected with MNPs versus control nanoparticles (WNPs). Increase was observed only in the presence of MNPs and not in the other control groups. (b) Summary of the fold change in corticosterone level when averaging post stimulation values versus pre-stimulation level in MNPs injected adrenals versus control particles (WNPs). (c) c-Fos expression in the injected area of MNPs. Green-c-fos, blue-DAPI. Scale bar=100 µm (d) Quantification of c-Fos expression in the injected area when comparing MNPs injection versus control (WNPs).

CONTRIBUTION OF THE PROPOSAL FOR A BETTER WORLD

I propose to develop a magnetic system that allows remote control on transplanted cells without the need to activate the organ itself. The magnetic system with the suggested magnetic gel and magnetic coil is suitable for various electrogenic cells that express heat sensitive or mechanosensitive ion channel[15] with high relevance to gastrointestinal tract [16] and pancreas[17]. This project is multidisciplinary and involves collaboration between biophysics of ion channels, nanomaterials and magnetic coils design. The magnetic stimulation parameters are safe and due to the magnetic susceptibility of tissues, it allows deep penetration to deep organs without further damage to the surrounding tissues.

As a proof of principle, I will demonstrate the ability to control remotely the release of the stress hormone cortisol, for treatment of imbalance in cortisol levels, relevant for mental health disorders such as PTSD and depression. The current therapies for mental health disorders are still lacking and the involvement of stress hormones contribution to the development of the disease requires further investigation. This research will pave the way to new approaches that can be multiplexed to control different cells[18] and can lead to future treatments, which can be drugs free with minimal side effects.

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13. Christiansen MG, Howe CM, Bono DC, Perreault DJ and Anikeeva P. Practical methods for generating alternating magnetic fields for biomedical research. *Review of Scientific Instruments*. 2017;88:084301.
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Dekel Rosenfeld - CV

dekelr@tauex.tau.ac.il; dekeld301@gmail.com

ACADEMIC APPOINTMENTS

Tel Aviv University

Senior Lecturer — Biomedical Engineering Department — 2022-current

Massachusetts Institute of Technology

Research Scientist — Research Laboratory of Electronics, McGovern Institute for Brain Research — 2020-2021

Postdoctoral Associate — Research Laboratory of Electronics,McGovern Institute for Brain Research — 2016-2020

Technion, Israel Institute of Technology

Postdoctoral Scholar — Biomedical Engineering Department — 2014-2015

EDUCATION

Technion, Israel Institute of Technology

Ph.D. in Biomedical Engineering — 2009-2014

M.Sc. in Biomedical Engineering — 2008-2009

B.Sc. in Biomedical Engineering, **cum laude** — 2003-2007

HONORS

Zuckerman Faculty Scholars — 2021

Travel grant award for postdoctoral fellows, Ilanit — 2020

NIH BRAIN Initiative Trainee award — 2018

Israel women in science award VATAT — 2017,2018

MIT-Technion Fellowship for postdoctoral research — 2016-2018

Katzir Fellowship for short term internship abroad, Boston, MA. — 2012

Ed Sattel fellowship for outstanding PhD students — 2008-2013

Dean's list for academic achievement for 5 semesters of undergraduate studies at the Technion — 2003-2007

Award of the Israel Stem Cell Society — 2013

Excellence in Teaching Award of the Technion — 2012, 2013

Diploma with honors (**cum laude**), Biomedical Engineering Department, Technion — 2007

TEACHING EXPERIENCE

Guest lecture, MIT course 3.001 "Intro Materials Science & Engineering" — 2019-2021

Guest lecture, MIT course 9.123 / 20.203 "Neurotechnology in action" — 2018,2019

Teaching assistant, "Transport phenomena in physiological systems", Technion — 2009-2013

Teaching assistant, "Heat transfer in biological systems", Technion — 2011,2012

Lab instructor, "Mechanical properties of tissues", Biomedical Engineering Department, Technion — 2009,2010

MENTORING EXPERIENCE

Supervised 4 undergraduate students in the MIT UROP program. Anikeeva lab. MIT — 2016-2020

Supervised a graduate student from the MIT-Imperial college program. Anikeeva lab, MIT — 2017-2018

Supervised an undergraduate student in MIT Summer Research Program (MSRP) — 2017

Supervised an undergraduate student from Georgia Tech in the summer research program — 2016

Supervised 3 projects for undergraduate thesis projects. Technion (4 students) — 2011-2013

PROFESSIONAL DEVELOPEMNT (selected)

Member: Materials Research Society, Society for Neuroscience, Biomedical engineering society — 2017-2019

MIT Kaufman Teaching Certificate Program, Massachusetts Institute of Technology — 2017

Member, Tissue Engineering and Regenerative Medicine International Society (TERMIS) — 2008-2012

Teaching assistant qualification program, Technion - Israel Institute of Technology — 2009

PUBLICATIONS (selected out of 24)

1. Sarah-Anna Hescham, Po-Han Chiang, Danijela Gregurec, Junsang Moon, Michael G Christiansen, Ali Jahanshahi, Huajie Liu, **Dekel Rosenfeld**, Arnd Pralle, Polina Anikeeva, Yasin Temel. 2021. Magnetothermal nanoparticle technology alleviates parkinsonian-like symptoms in mice. Nature communications. 12 (1), 1-10
2. Marc-Joseph Antonini, Atharva Sahasrabudhe, Anthony Tabet, Miriam Schwalm, **Dekel Rosenfeld**, Indie Garwood, Jimin Park, Gabriel Loke, Tural Khudiyev, Mehmet Kanik, Nathan Corbin, Andres Canales, Alan Jasanoff, Yoel Fink, Polina Anikeeva. 2021. Customizing MRI-Compatible Multifunctional Neural Interfaces through Fiber Drawing. Advanced Functional Materials. 2104857
3. Anthony Tabet, Marc-Joseph Antonini, Atharva Sahasrabudhe, Jimin Park, **Dekel Rosenfeld**, Florian Koehler, Hyunwoo Yuk, Samuel Hanson, Jordan A Stinson, Melissa Stok, Xuanhe Zhao, Chun Wang, Polina Anikeeva. 2021. Modular integration of hydrogel neural interfaces. ACS Central Science. 7, 9, 1516–1523
4. Dena Shahriari*, **Dekel Rosenfeld*,** Polina Anikeeva. Emerging frontier of peripheral nerve and organ interfaces. Neuron. In press *Equal contribution
5. **Dekel Rosenfeld**, Alexander W. Senko, Junsang Moon, Isabel Yick, Georgios Varnavides, Danijela Gregureć, Florian Koehler, Po-Han Chiang, Michael G. Christiansen, Lisa Y. Maeng, Alik S. Widge and Polina Anikeeva. 2020. Transgene-free remote magnetothermal regulation of adrenal hormones. Science Advances. 6 (15), eaaz3734.
6. Jimin Park, Kyoungsuk Jin, Atharva Sahasrabudhe, Po-Han Chiang , Florian Koehler, **Dekel Rosenfeld**, Joseph Maalouf, Siyuan Rao, Tomo Tanaka, Tural Khudiyev, Yoel Fink, Karthish Manthiram and Polina Anikeeva. 2020. In situ electrochemical generation of nitric oxide for spatiotemporally precise neuronal modulation. Nature nanotechnology. 15 (8), 690-697.
7. Junsang Moon, Michael Christiansen, Siyuan Rao, Colin Marcus , David Bono, **Dekel Rosenfeld** ,Danijela Gregurec ,Georgios Varnavides, Po-Han Chiang, Seongjun Park and Polina Anikeeva. 2020. Magnetothermal multiplexing for selective remote control of cell signaling. Advanced Functional Materials. 30 (36), 2000577.
8. Danijela Gregurec, Alexander Senko, Andrey Chuvilin, Pooja Reddy, Ashwin Sankararaman, **Dekel Rosenfeld**, Po-Han Chiang,; Francisco Garcia, Ian Tafel, Georgios Varnavides, Eugenia Ciocan, Polina Anikeeva. 2020. Tuning the magnetic vortex state in magnetite nanodiscs for remote control of biological signaling. ACS Nano. 14 (7), 8036-8045.
9. Jonathan Avesar, **Dekel Rosenfeld**, Marianna Truman-Rosentsvit, Tom Ben Arye, Yuval Geffen, Moran Bercovici, and Shulamit Levenberg. 2017. Rapid phenotypic antimicrobial susceptibility testing using nanoliter arrays. Proc Natl Acad Sci U S A. 114 (29), E5787-E5795.
10. **Dekel Rosenfeld**, Shira Landau, Yulia Shandalov, Noa Raindel, Erez Shor, Yaron Blinder, Herman Vandenburgh, David Mooney and Shulamit Levenberg. 2016. Morphogenesis of 3D vascular network is .regulated by tensile forces. Proc Natl Acad Sci U S A. 113(12): 3215–322.
11. **Dekel Dado-Rosenfeld**, Itai Tzchori, Amir Fine, Limor Chen-konak and Shulamit Levenberg. 2014. Tensile forces applied on a cell-embedded 3D scaffold can direct early differentiation of embryonic stem cells toward the mesoderm germ layer. Tissue engineering Part A. 21 (1-2), 124-133.
12. **Dekel Dado** and Shulamit Levenberg. 2009. Cell–scaffold mechanical interplay within engineered tissue. Seminars in Cell and Developmental Biology. 20 (6), 656-664.

Patents

1. J Avesar, S Levenberg, **D Rosenfeld**, YJ Blinder. Antimicrobial susceptibility test kits. US Patent App. 16/486,879
2. P Anikeeva, **D Rosenfeld**, A Widge. Therapeutic uses of controlled adrenal release. University of Minnesota patent.

SELECTED ABTRACTS AND INVITED TALKS (selected out of 21)

1. Invited seminar, NYU Langone Health, New York, NY, September 2021
2. Oral presentation: “Neurotech in Action” symposium, MIT, Cambridge, MA, 2020
3. Oral presentation: 2019 Biomedical Engineering society conference, Philadelphia, PA, 2019
4. Research highlight talk: 2018 BRAIN Initiative PI Meeting, DC, 2018
5. Oral presentation: 2018 Material Research Society, Phoenix, AZ, 2018
6. Invited speaker: 2017 Mayo Clinic Symposium on the BRAIN Initiative, Rochester, MN, 2017
7. Oral presentation: 4th TERMIS World Congress. Boston, MA, USA. September 2015
8. Oral presentation: 5th International Conference on Tissue Engineering, Kos, Greece, June 2014

BUDGET

	Requested	Matching	Total
Lab manager	6,000$	2,000$	8,000$
Postdoc	21,000$	7,000$	28,000$
Shared facilities	9,000$	3,000$	12,000$
Equipment	30,000$	10,000$	40,000$
Consumable	6,000$	2,000$	8,000$
Publications	3,000$	1,000$	4,000$
Total	75,000$	25,000$	100,000$

BUDGET JUSTIFICATION

Personnel

The team will include the PI, a lab manager and a postdoc. Due to the multidisciplinary nature of the project, the background of the team members will be from different disciplines.

The PI will supervise the work and perform training on nanoparticle synthesis and electronic equipment setup. The lab manager will be responsible for ordering electronic equipment, supplies and consumable, day-to-day lab operation, establishing biological experiments and assist with protocols and microscopy.

A postdoc will be hired for this project. The postdoc will be with engineering background and knowledge in materials design or electronic design. The postdoc will functionalize the nanoparticles, establish the nanocomposites, test them with cell cultures and construct the magnetic setup.

The funds for the lab manager are based on dedicating 15% of the time for this project. The funds requested for the postdoc are according to the standard fellowship at Tel Aviv University.

Shared facilities

The equipment in the Center for Nanoscience and Nanotechnology in Tel Aviv University will be used for nanoparticles and nanocomposites characterization (electron microscopy, vibrating sample magnetometer and thermogravimetric analysis).

Equipment

The budget will be used to purchase all the magnetic setup including: electronic components for the RLC circuit (capacitors, resistors etc.), the gapped toroidal coil, power supply, function generator, and oscilloscope. Moreover, we will purchase an optical based temperature probe and infra-red camera.

Consumable

The budget will be used to purchase general lab supply as well as biological and chemical materials for nanocomposites synthesis and biological work with cell cultures. This include polymers, solvents and chemical for the chemical work and biological reagents (cell media, Alamarblue dye, reagents for cell dissociation).

Publications

This project is expected to produce 1-2 publications in high impact open access journals and the budget will be used for publication costs and manuscript editing.

From the desk of Prof. Mickey Scheinowitz
Director, Sylvan Adams Sports Institute

משולחנו של פרופ' מיקי שיינוביץ
מנהל, מכון סילבן אדמס לספורט

Iby and Aladar Fleischman
Faculty of Engineering
Tel Aviv University

הפקולטה להנדסה
ע"ש איבי ואלדר פליישמן
אוניברסיטת תל-אביב

Feb 14th, 2022
Prof. David Mendelovitch
Director
Zimin Institute
Faculty of Engineering
Tel Aviv University

Dear David,

Re: Endorsement letter for Dr. Dekel Rosenfeld

I hereby support and endorse the application of Dr. Dekel Rosenfeld on "**Magnetic system for remote control on cortisol release from bioelectronic implants**" submitted to the 2022 'Zimin Institute for Engineering Solutions Advancing Better Lives' call.

Dr. Rosenfeld is a new faculty member in Biomedical Engineering. Her proposal focus on the development of a new strategy to treat neuro-adrenal disorders using newly developed bio-electromagnetic implants and external stimulation.

The proposal fits with the 2022 Zimin's call for medical equipment and sensing.

I wish Dekel good luck with her application.

Sincerely yours,

Prof. Mickey Scheinowitz
Chair; Department of Biomedical Engineering
The Iby and Aladar Fleischman Faculty of Engineering
Tel Aviv University

קריית האוניברסיטה, ת"ד 39040, תל אביב 6139001 ● טל' 03- 6408123
Tel Aviv University, P.O.B. 39040, Ramat Aviv, Tel Aviv 6139001, Israel ● Tel: 972-3-6408123