Report

on

Brain Research

supported by

March 2017

Brain Research

The Adelis Foundation has helped enhance brain research at the Technion in multiple ways, including collaborations with the Weizmann Institute of Science, research activities at the Technion, the establishment of an imaging core facility and the refurbishment of the laboratory of Prof. Jackie Schiller.

The activities supported fully or partially by The Adelis Foundation are detailed in this report.

Collaborative Work Technion – Weizmann
Recent Grants

Does Social Status Affect Immune Activity?

Asst. Prof. Asya Rolls (Technion) and Prof. Tali Kimchi (Weizmann).

Increasing evidence correlates personality traits with changes in immune activity. These observations raise multiple questions regarding the interaction between the immune and the cognitive/emotional profile.

For example:

- What comes first?
- Does personality dictate a specific immune profile or can immunity alter personality?
- Can behavior alter immunity?
- Is social status correlated with a specific immune profile?

Moreover, do we have very limited understanding of the neuronal mechanisms connecting between the brain and immunity?

To address these questions, we developed a new experimental paradigm based on the system for automated characterization of social behaviors and dominance hierarchy in a group of mice in a semi-natural environment, as established by the Kimhi Laboratory (Weissbrod et al 2013, Nature Communication).

This enables us to determine the social behavioral profile of individual mice and correlate it with an immune profile. The immune profile is determined by a multifactorial, state of the art tool, CyTOF, based on tens of markers in the immune system. So far, we have been able to establish the system and run four individual experimental arenas. We gathered a significant amount of data that enables us to evaluate the quality of the data and to frame specific hypothesis for analysis.

Things our Brain Knows but We Do Not

Prof. Shimon Marom (Technion) and Dr. Amos Arieli (Weizmann).

In this project, the responses of human subjects to repeated stimuli tend to vary from one trial to another. While traditionally considered a reflection of “machine noise” (i.e. imprecise nature of brain processes and elements), we have decided to explore the possibility that response variations can tell us something deeper about the very nature of cognitive processes involved in a subject’s attempts to “figure-out” its surroundings.

To this end, we developed a paradigm that enables the study of the neural and cognitive processes underlying reasoning during the emergence of perceptual awareness in humans, by continuously measuring sensory sensitivity, human eye movement and

mass brain-activity, while the sensory stimuli and behavioral performance are manipulated by real-time closed-loop designs. The results are encouraging.

Traffic of Mitochondria and Proteins along Neurons

Assoc. Prof. Yoav Arava (Technion) and Prof. Abraham Yaron (Weizmann).

Neurons are long and dispersed, and need to maintain high-energy demands, even at the most distant synapses. Our collaborative project aims to reveal how energy is transported and maintained at distant sites along neurons. Mitochondria (the cellular energy factories) and their associated factors are isolated from axons of newly born mice. We apply innovative technologies to characterize the content and function of these energy producers.

This will provide important insight into energy transport and maintenance, and more broadly about information transfer within the nervous system.

Searching for Stable Mental Schemas in Neural Codes for Long Term Memory

Asst. Prof. Omri Barak (Technion) and Dr. Yaniv Ziv (Weizmann).

Our day-to-day experience with navigation is strongly associated with the concept of a map. Accordingly, most models of the neural basis of navigation are focused around the neural representation of maps. This approach is, of course, supported by the finding of place cells and grid cells in the hippocampal formation. In this project, we decided to challenge this common assumption, by studying whether navigation tasks can be accomplished without explicit representation of cognitive maps.

Surprisingly, we found that a model network was able to learn a simple navigation task, without any internal representation of a cognitive map. These results provide a new lens through which to view the neural basis of navigation.

Novel Methods for Quantitative Measurement of GABA In-Vivo

Asst. Prof. Itamar Kahn (Technion) and Dr. Assaf Tal (Weizmann).

Kahn and Tal are developing a novel method to image the brain of individuals with a disruption to one of the major regions in the brain, the striatum, responsible for motor and reward processing in the brain. Using MRI, a non-invasive method used extensively in humans, and a new imaging protocol that was developed by Dr. Assaf Tal to image activity of a class of neurons (called spiny neurons, that comprise 95% of the neurons in the striatum), Dr. Tal and Dr. Kahn aim to identify the disruption of this region which has been recently linked to autism.

Dr. Kahn plans to use this approach to test whether children with a genetic disorder can be diagnosed using this novel approach.

Space Coding in the Avian Hippocampal Formation

Assoc. Prof. Yoram Gutfreund (Technion) and Prof. Nachum Ulanovsky (Weizmann).

The learning and representation of space has been studied extensively in the past three decades, leading to the recent Nobel Prize in Physiology or Medicine. However, one important question remained unresolved: Is the role of the hippocampus in space processing limited to mammals or can we find its origins in other vertebrates?

In October 2015, we began an extensive study of space processing in the non-mammalian hippocampus.

This study is an Adelis funded project, aimed to combine our two labs. Nachum Ulanovsky's lab contributes its expertise in studying space processing in bats, as well as the unique techniques developed in the lab to record single units from freely flying animals.

Yoram Gutfreund's laboratory contributes its expertise in electrophysiological and behavioral studies of birds, as well as its facilities for avian research. We study two species of birds, Japanese quail and barn owl. State of the art techniques for recording from freely behaving animals are applied in conjunction with a variety of spatial tasks. We are searching for place cells, spatial-view cells and other types of space representing cells.

We believe that this research will contribute significantly to our understanding of the evolutionary origins of space processing, as well as open new directions for studying mechanisms of space processing.

Conferences

Since our last report in 2016, we arranged a conference supported by the Adelis Foundation.

The title of the Conference was ***"Science and Engineering of Neural Systems"*** and was organized by Prof. Jackie Schiller and Asst. Prof. Itamar Kahn, both from the Technion's Ruth and Bruce Rappaport Faculty of Medicine.

The conference brought together researchers (as listed below) from 26 laboratories from the different engineering, life sciences and medical related faculties of the Technion, with the purpose of jump-starting the future brain center at the Technion.

Faculty of Biology

Prof. Benjamin Podbilewicz

Faculty of Biomedical Engineering

Prof. Shulamit Levenberg

Wolfson Faculty of Chemical Engineering

Assoc. Prof. Naama Brenner

Faculty of Education in Science and Technology

Dr. Tzipi Horowitz-Kraus

Viterbi Faculty of Electrical Engineering

Prof. Yonina Eldar
Asst. Prof. Guy Gilboa
Asst. Prof. Shahar Kvatinsky
Prof. Ron Meir
Asst. Prof. Amir Rosenthal
Asst. Prof. Ronen Talmon

William Davidson Faculty of Industrial Engineering and Management

Asst. Prof. Rakefet Ackerman
Prof. Ido Erev
Assoc. Prof. Eldad Yechiam

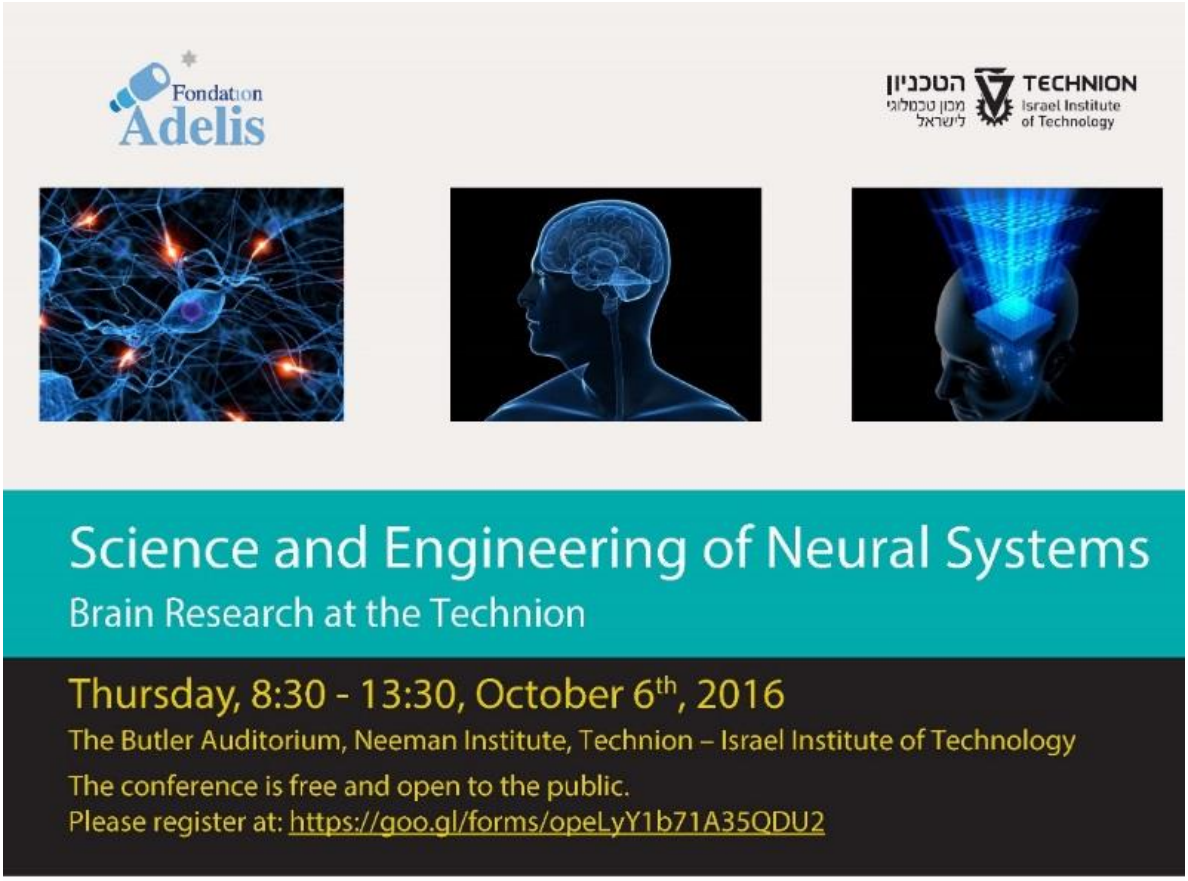
Faculty of Mechanical Engineering

Asst. Prof. Shelly Tzlil
Assoc. Prof. Alon Wolf
Assoc. Prof. Miriam Zacksenhous

Ruth and Bruce Rappaport Faculty of Medicine

Asst. Prof. Avraham Avital
Assoc. Prof. Dorit Ben-Shachar
Asst. Prof. Dori Derdikman
Assoc. Prof. Simone Engelender
Asst. Prof. Itamar Kahn
Prof. Shimon Marom
Asst. Prof. Asya Rolls
Prof. Jackie Schiller
Assoc. Prof. Yitzhak Schiller
Prof. Noam Ziv

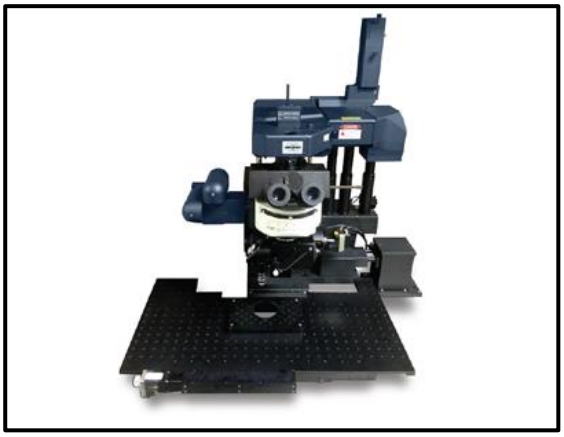
The following is the publicity poster from the Conference:



Adelis Advanced Imaging Facility

Establishing core facilities is an essential part of establishing the future brain research center at the Technion. The facility will include state of the art microscopes for in-vivo imaging, such as two photon microscopes, advanced photostimulation systems such as optogenetics and controlled compound uncaging and whole brain imaging such as the MRI. This facility is one of few in the entire world that will enable imaging from a single cell to an entire brain in mammals.

The Adelis Foundation is helping to establish an **Advanced Imaging Facility** by participating in the purchase of the state of the art two-photon in-vivo imaging microscope (see picture) with a contribution of $200,000.



The balance of funds needed for the purchase has been raised from other sources thanks to the lead of the Adelis Foundation.

The renovation of the special clean room for the microscope is about to start.

New Call for Joint Adelis Technion-Weizmann Research Grants

A new call for collaborative research proposals for the year 2017 will be issued shortly.

The call will encourage applications from proposals, which will show a large degree of innovation and synergism between the groups. We will also encourage the involvement of joint PhD students in the research. The aim will be to fund four suitable grants, which will be chosen through an unbiased peer review process.

Publications

The generous support of the Adelis Foundation accelerated the research of the brain research laboratories, and resulted in publications from multiple laboratories in high profile journals:

Sandler et al. (2016) “A novel form of local plasticity in tuft dendrites of neocortical somatosensory layer 5 pyramidal neurons,” Neuron.

Ben-Shaanan et al. (2016) “Activation of the reward system boosts innate and adaptive immunity,” Nature Medicine.

Bergmann et al. (2016) “The Organization of Mouse and Human Cortico-hippocampal Networks Estimated by Intrinsic Functional Connectivity,” Cerebral Cortex.

Barzelay et al. (2017) “A New Approach to Model Pitch Perception Using Sparse Coding,” PLoS computational Biology.

Washmut et al. (2017) “Distinct stimulus specific adaptation to visual and auditory motion direction in the owl's optic tectum,” European Journal of Neuroscience.

Khateb et al. (2017) "Feedforward motor information enhances somatosensory responses and sharpens angular tuning of rat S1 barrel cortex neurons."

Elife Korin et al. (under revision) “High-dimensional Mass Cytometry Characterization of the Brain’s Immune Populations”.

Shofty et al. (under revision) “Neurofibromin deficiency is linked to striatal dysfunction,” eNeuro.

Rivkind & Barak (under revision) “Local dynamics in trained recurrent neural networks,” PRL.

Xu & Barak (under review) “Marginal stability and dynamic timescales in single neuron excitability,” Journal of Neuroscience.

ADELIS FOUNDATION – Grant for Brain Diseases Program Financial Statement						
	YEAR 1 2012 $	YEAR 2 2013 $	YEAR 3 2014 $	YEAR 4 2015 $	YEAR 5 2016 $	TOTAL $
INCOME						
Grant received	500,000	500,000	500,000	500,000	500,000	2,500,000
DISTRIBUTION OF FUNDS						
Research Grants	100,000		50,000	200,000	400,000[1]	750,000[2]
Refurbishment Grant - Cortical Comp. Laboratory	400,000	250,000	52,000	50,000		752,000
Allocation for Advanced Imaging Facility					203,380	203,380
Core Services for the support of research		40,000	(40,000)[3]		791,120	791,120
Future Research Proposals		210,000	438,000	246,500	(894,500)[4]	-
Conference Expenses				3,500		3,500
Total Distribution	**500,000**	**500,000**	**500,000**	**500,000**	**500,000**	**2,500,000[5]**
BALANCE OF FUNDS	-	-	-	-	-	-

[1] The amount of $400,000 relates to $200,000 allocated to four research proposals for 2016 and $200,000 set aside for four research proposals for 2017.

[2] Research grants were distributed as follows:

2012	$
Prof. Dvir Yelin, Technion and Prof. Noam Sobel, Weizmann Institute	50,000
Asst. Prof. Itamar Kahn, Technion and Prof. Ilan Lampl, Weizmann Institute	50,000
2014	
Asst. Prof. Omri Barak, Technion and Dr. Yaniv Ziv, Faculty of Biology, Weizmann Institute	50,000
2015	
Asst. Prof. Asya Rolls, Technion and Dr. Tali Kamchi, Department of Neurology, Weizman Institute	50,000
Assoc. Prof. Yoram Gutfreund, Technion and Prof. Nahum Ulanovsky, Weizmann Institute	50,000
Prof. Yitzhak Schiller, Technion and Prof. Raphael Malach, Weizmann Institute	50,000
Prof.Shimon Marom, Technion and Prof. Dov Sagi and Dr. Amos Arieli, Weizmann Institute	50,000
2016	
Prof. Prof. Benjamin Podbilewicz and Prof. Ehud Ahissar, Weizmann Institute	50,000
Assoc. Prof. Yoav Arava, Technion and Prof. Avraham Yaron, Weizmann Institute	50,000
Prof. Noam Ziv, Technion and Prof. Elad Moshe Sheindman, Weizmann Institute	50,000
Asst. Prof. Itamar Kahn, Technion and Dr. Assaf David Tal, Weizmann Institute	50,000
2017	
Yet to be allocated	200,000

[3] $40,000 was re-allocated from core services to future research proposals.

[4] This amount of $894,500 and the 2016 grant of $500,000 was allocated as follows: Research Grants $400,000; Refurbishment Grant –Advanced Imaging Facility $203,380; and Core Services $791,120.

[5] At the end of 2017 we will present a final statement of account for this total amount of $2,500,000.

The Technion

expresses appreciation to

for its support of this project

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