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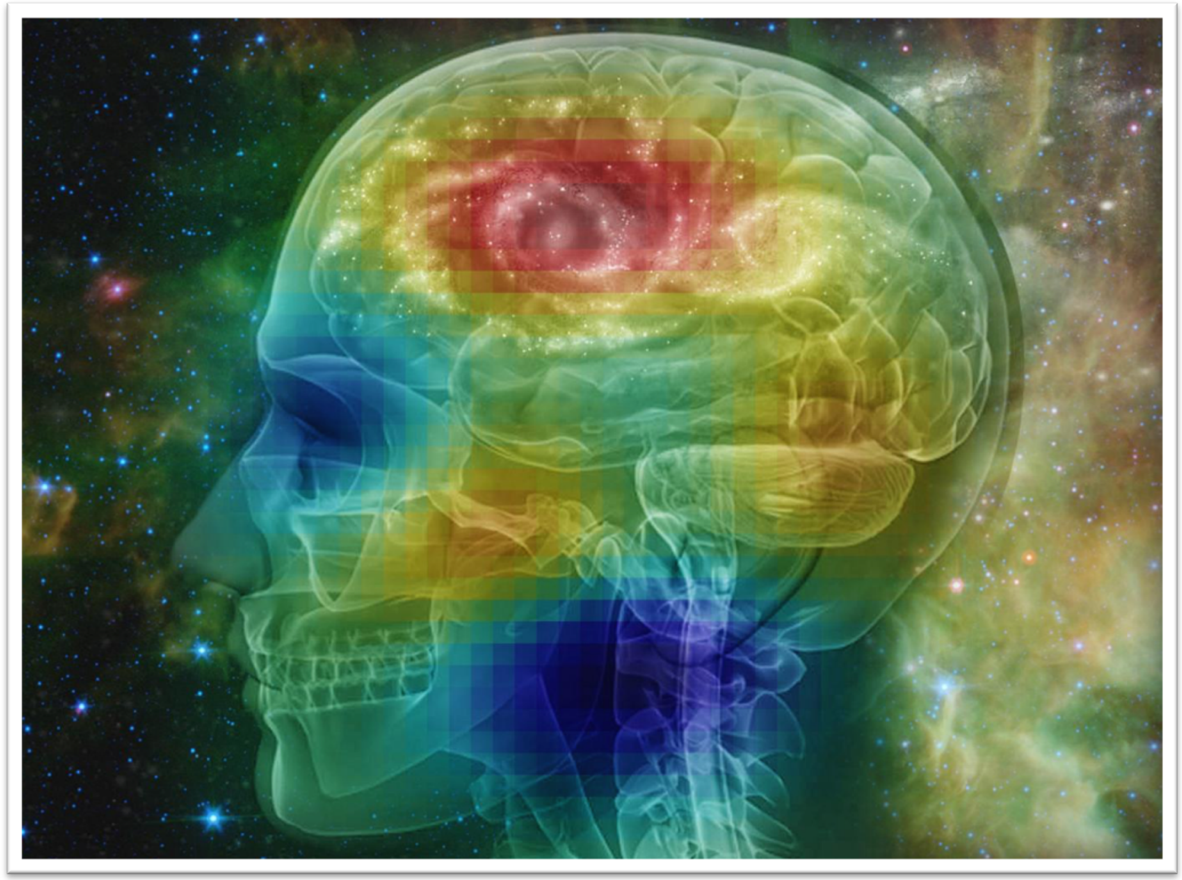
Overview of JPL, current Biomedical Engineering Projects at JPL, and JPL/GAMC collaboration



Dr. Marco B. Quadrelli

with contributions by Rao Surampudi, Hari Nayar, Chris Assad, Adrian Stoica

Jet Propulsion Laboratory
Pasadena, CA 91109

September 27, 2018

Outline

- Background
- Biomedical Engineering Projects at JPL
  - Past Projects, Current Projects, Projects in Formulation
- Summary of current JPL/GAMC collaboration

JPL is part of NASA *and* Caltech

- Federally-funded (NASA-owned) Research and Development Center (FFRDC)
- University Operated (Caltech)
- $2.3B Business Base
- >5,600 Employees

- 167 Acres (includes 12 acres leased for parking)
- 139 Buildings; 36 Trailers
- 673,000 Net Square Feet of Office Space
- 906,000 Net Square Feet of Non-Office Space (e.g., Labs)

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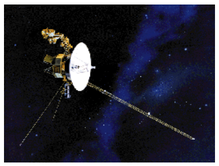
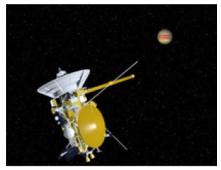
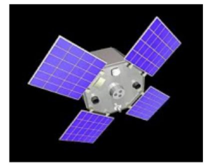
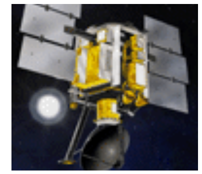
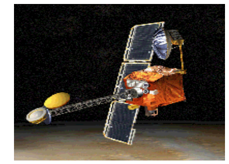
Over 20 Spacecraft and 12 Instruments Across the Solar System and Beyond


Two Voyagers (1977)

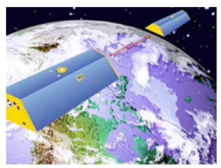

Cassini (1997)

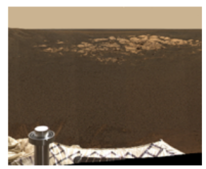

ACRIMSAT (1999)


QuickSCAT (1999)

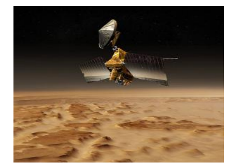

Mars Odyssey (2001)

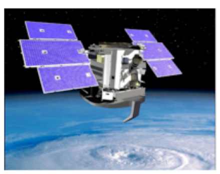

Jason 2 (2008)


GRACE (2002)

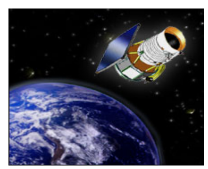

Opportunity (2003)

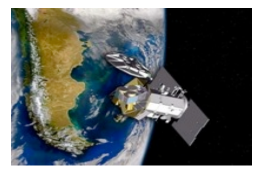

Spitzer (2003)

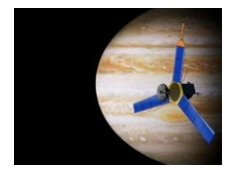

Mars Reconnaissance Orbiter (2005)


CloudSat (2006)


Dawn (2007)


NEOWISE (2009)


Aquarius (2011)


Juno (2011)


Curiosity (2011)


NuSTAR (2012)


OCO-2 (2014)


SMAP (2015)

Instruments:

Earth Science

- MISR (1999)
- AIRS (2002)
- TES (2004)
- MLS (2004)
- ASTER (2009)
- OPALS (2014)
- RapidScat (2014)

Planetary

- MARSIS (2003)
- MIRO (2004)
- Diviner (2004)
- TLS (2011)
- Chemin (2011)

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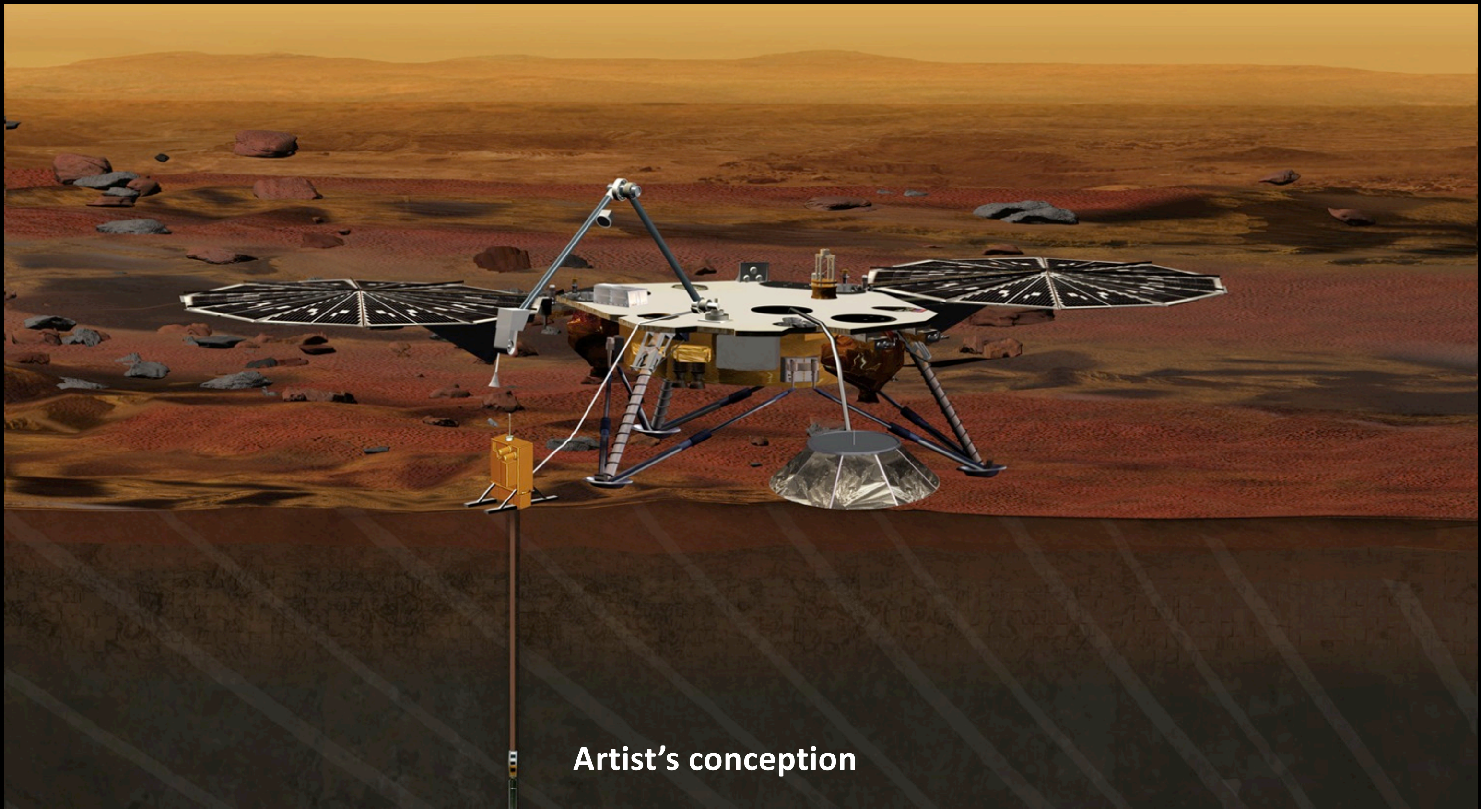
Missions in Development

InSight



Artist's conception

Missions in Development

Psyche

Artist's conception

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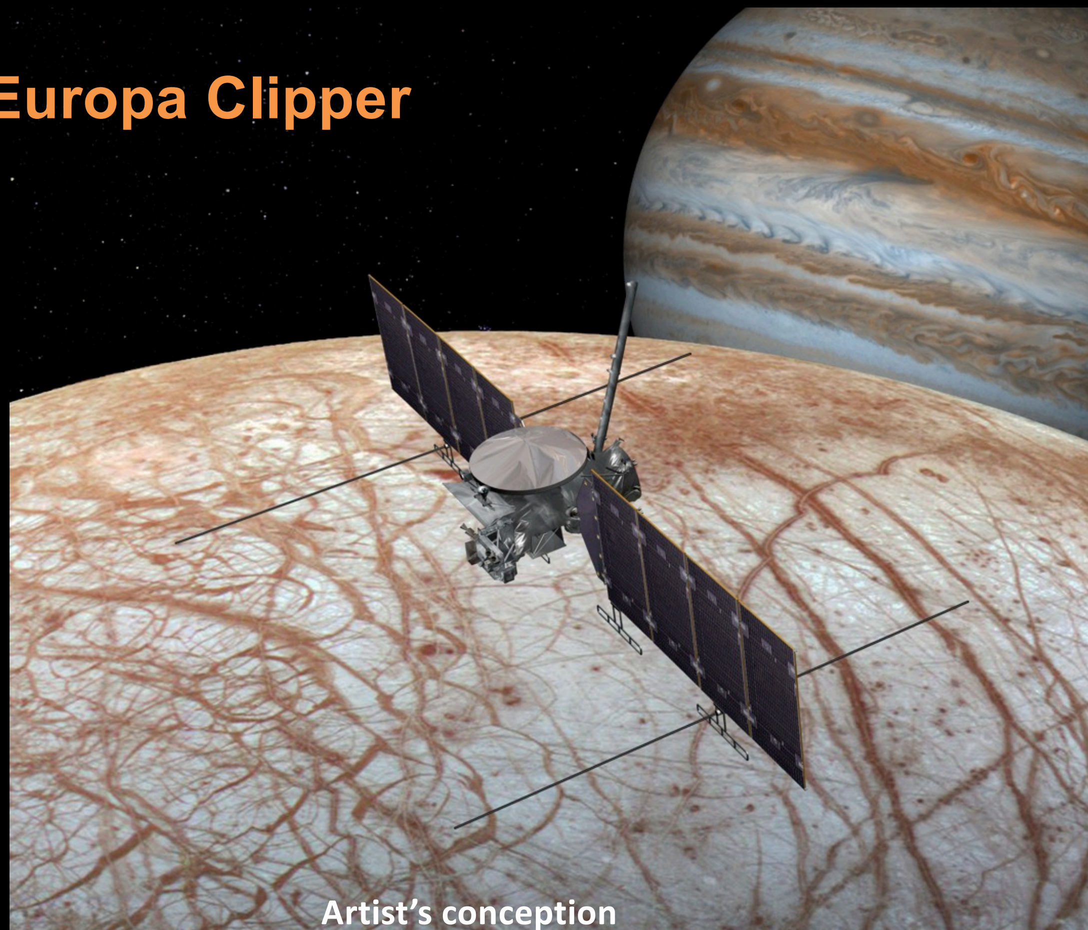
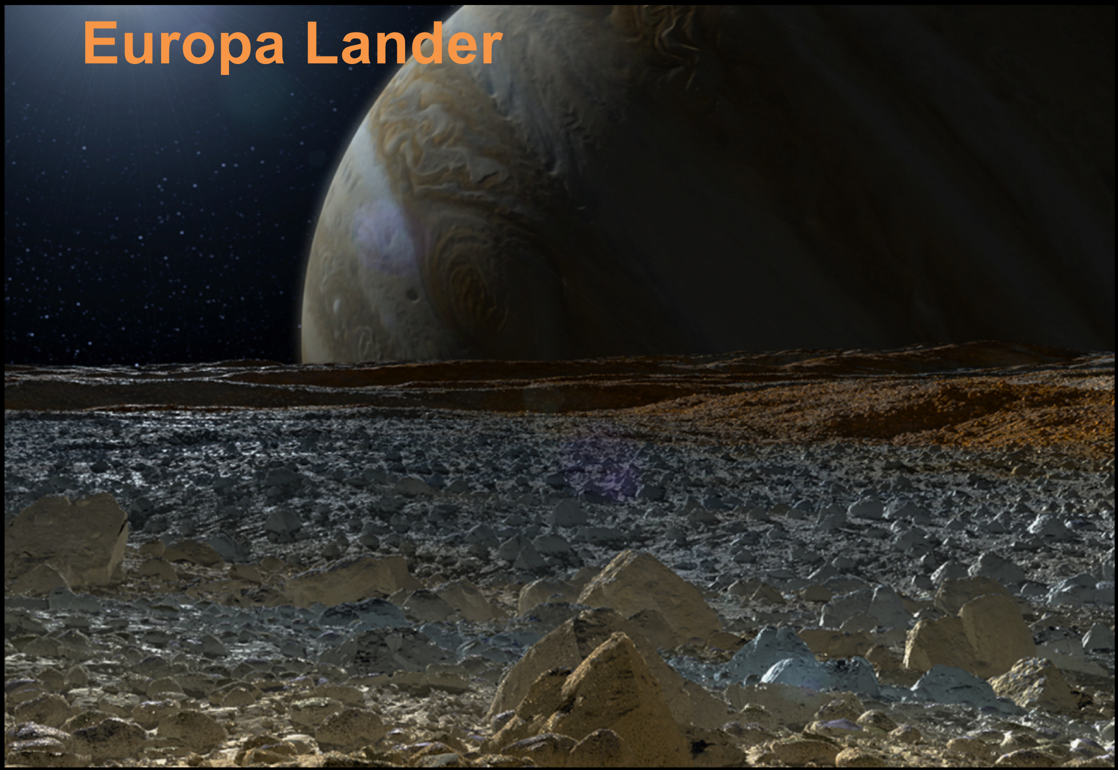
Missions in Development:



Artist's conception

Mission Studies

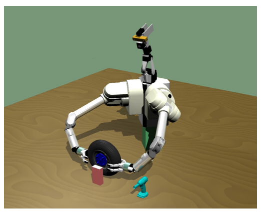


Artist's conception

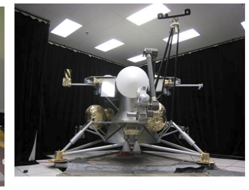
A snapshot of JPL Robotics

Perception for Legged Vehicles

Autonomous Manipulation

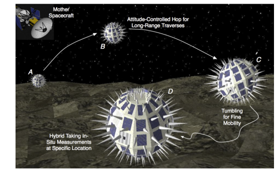


Venus Exploration Mission Concepts

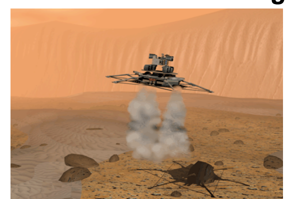


Mars/Lunar Sampling Mission Concepts

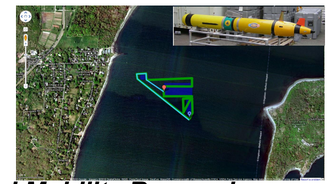
Comet Touch-and-Go and Hopping



Terrain-relative navigation



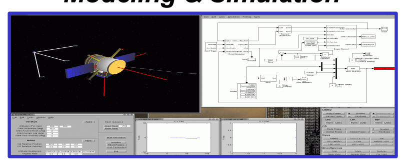
Ocean Mobility Research



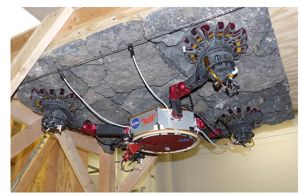
Axel rover

Microgravity M&M Testbed

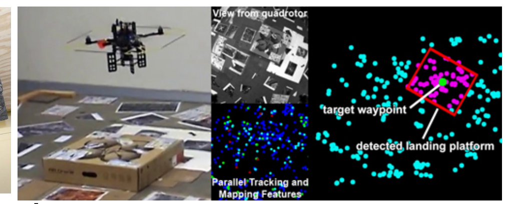
Physics-based Modeling & Simulation



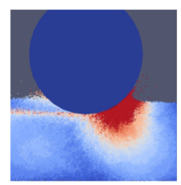
Gripping Foot Mechanisms

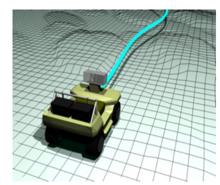


Aerial Mobility Research

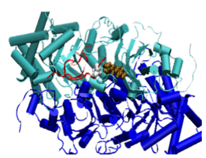


Ground Mobility Research



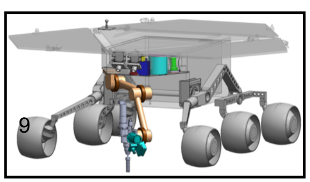


Human-robot Interfaces



Power Efficient Fast Traverse For Planetary Rovers

Rock Sampling and Containerization



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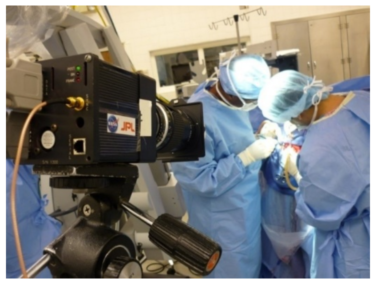
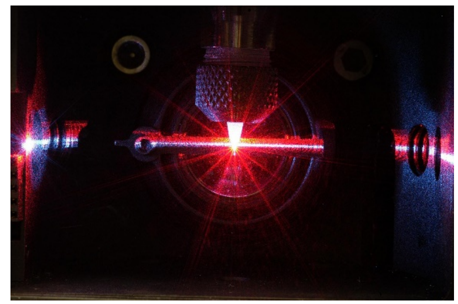
JPL Capabilities in Biomedical Engineering

Sensors



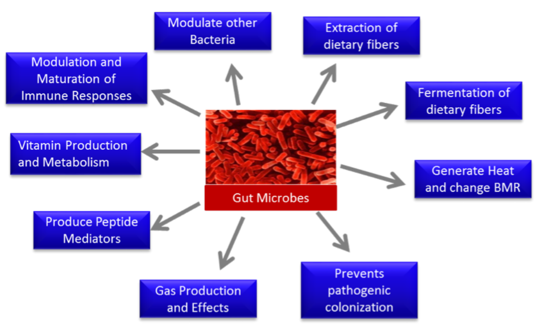
Detectors & Cameras



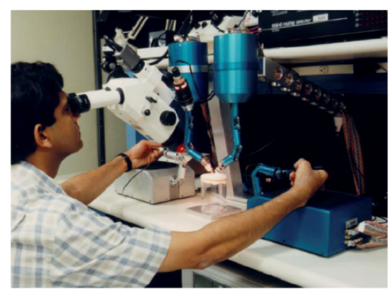
Instruments

Materials

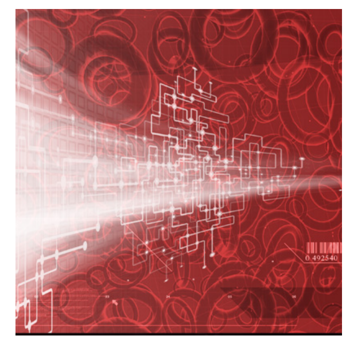
Planetary Protection



Microbe Interactions

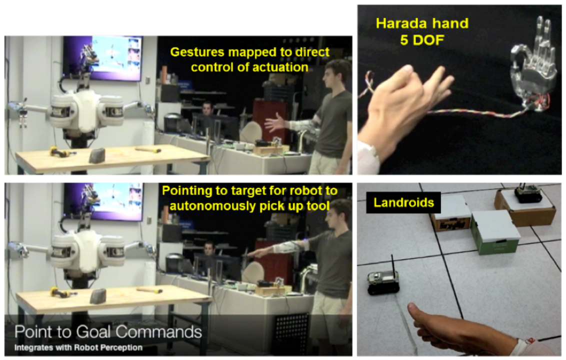


Robotic Surgery

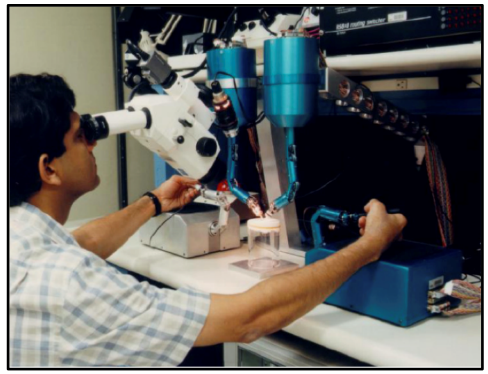


Data Science Technologies

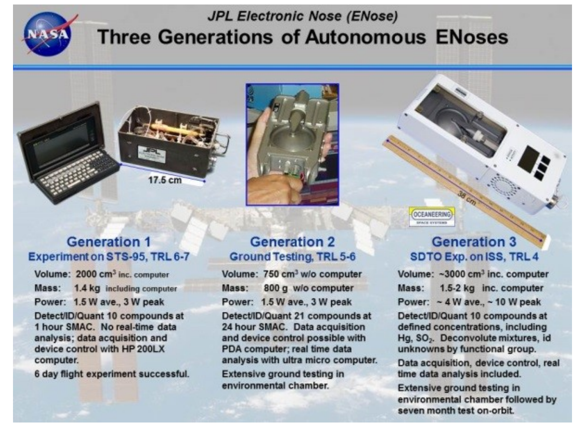
Biomedical Engineering Projects- Past & Present



BioSleeve Gesture Control Interface



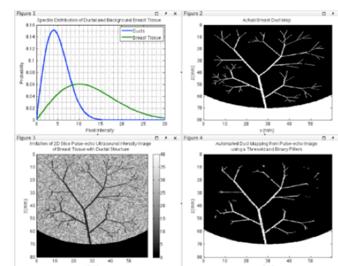
Robot-assisted Micro-Surgery Concept for Vitreo-retinal Surgery.



Electronic Nose

Rapid Microbial Testing for Tissue Processing

FINDER Project



Breast Duct Mapping

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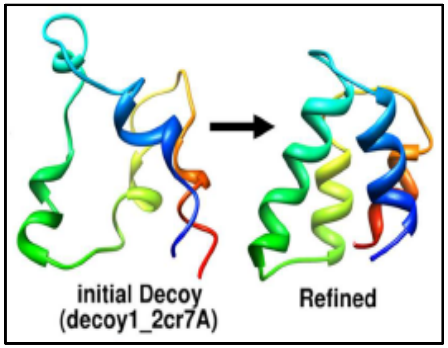
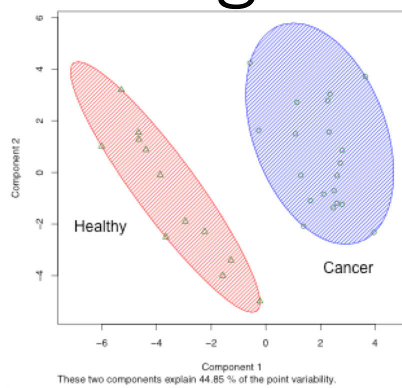
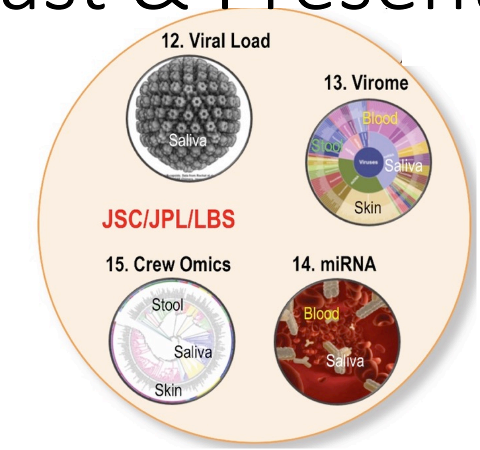
Biomedical Engineering Projects- Past & Present



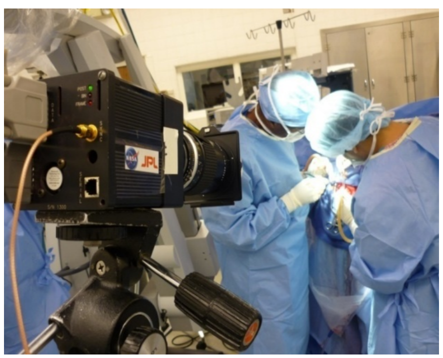
Protein Structures Using GNEIMO Computational Methodologies



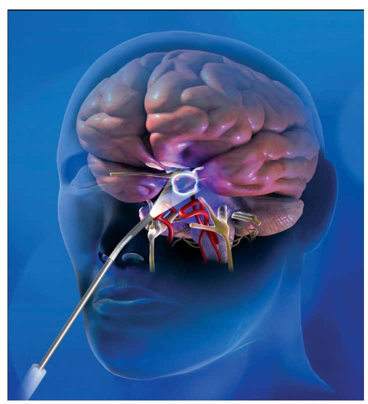
Breast Cancer & Microbiome



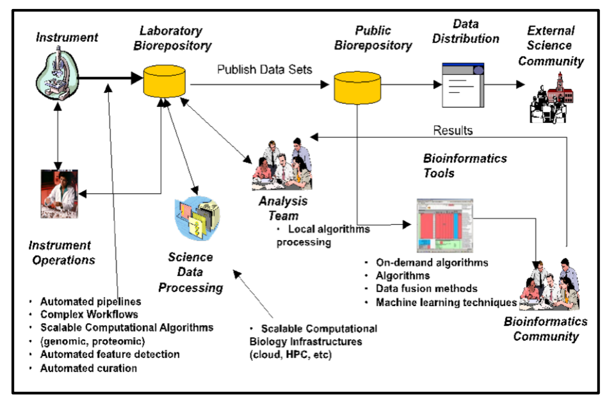
Omics in Space



Detectors & Cameras



3D Endoscope Technology



Cancer Biomarkers

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Collaborations and Working with Community

AlloSource
Doing More With Life

Medtronic

Dr. Susan Love Research Foundation
For a future without breast cancer

Marvel Innovations

Vydiant

Early Detection
Research
Network

California Institute of Technology 1891

The University of California Davis
Let there be light

Loma Linda University Health
To make man whole

City of Hope

Adventist Health Glendale

Cedars-Sinai

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NASA proposal opportunity

TRANSLATIONAL RESEARCH INSTITUTE FOR SPACE HEALTH

About the Solicitation	**TRISH** is seeking and funding emerging scientific and **Biomedical Research Advances for Space Health (BRASH)**, disruptive technologies, therapies, and new approaches that reduce risks to human health and performance during deep space exploration. Annual budget up to $400,000 with a project duration of 2 years
Areas of Interest	BRASH solicitation is solely focused on the following six topics: Predictive algorithms of health, behavior, and medical events Improving resilience through nucleotide-based therapy Non-pharmacological improvement of human performance Multipurpose edible plants for spaceflight applications New materials for shielding medications Test your expired medications
Schedule	The solicitation is composed of 4 phases. Phase 1 includes the release, pre-proposal webinar, and three-page proposal (Step-1). In Phase 2, select Step-1 proposers will be invited to submit a full-length Step-2 proposal. In Phase 3 proposals are reviewed for scientific, technical, and programmatic merit. Awardees are notified in Phase 4. **March 16, 2018** BRASH 1801 Release **April 27, 2018** Step-1 Notifications **June 25, 2018** 5:00 pm EST Step-2 Proposals Due **November 2018** Selection Announcement STEP-1 → STEP-2 → REVIEW → SELECTION **March 28, 2018** 2-3:00 pm EST Pre-Proposal Webinar **April 16, 2018** 5:00 pm EST Step-1 Proposals Due
About TRISH	At TRISH, we focus on approaches that NASA needs and is not currently pursuing. We seek high risk, high reward, high quality and efficient solutions that can be adapted (or translated) for use in space. Cool, right?! Find out more information about TRISH at bcm.edu/spacehealth.
Why TRISH?	TRISH offers: • Non-dilutive federal funding • Access to spaceflight and space analogs • New partnerships through our virtual network • High risk threshold
Eligibility	Personnel employed by U.S.-based institutions or companies may apply. All organizations must register (or already be registered) with the System for Award Management (SAM).
Contact	Questions regarding BRASH1801? Not sure whether or how your research could apply to the challenges astronauts face in space? We can help! Contact emmanueo@bcm.edu about BRASH1801 or to learn about other TRISH funding opportunities.

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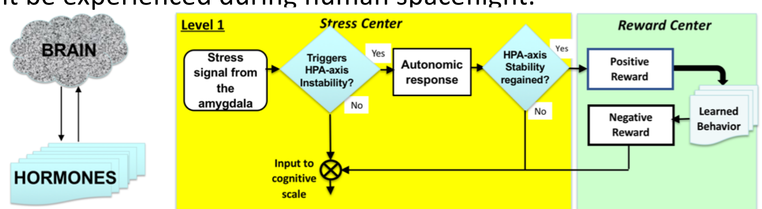
California Institute of Technology

A Resilience Algorithm: modeling HPA-axis correlations with ACEs and epigenetic expression

Team: Jet Propulsion Laboratory – Loma Linda University (LLU–Lee Berk, Rhonda Spencer, Warren Peters); Adventist Health Glendale (AHGL–Bruce Nelson); California Institute of Preventive Medicine (CIPM–Vincent Felitti); Cousins Center for Psychoneuroimmunology (UCLA–Steve Cole); Duke University Department of Psychiatry and Behavioral Sciences (Duke–Harold Koenig); California Institute of Technology (JPL–Marco Quadrelli).

Background: Humans need to maintain HPA-axis stability is supported by successive layers of feedback systems that can interact to exert either stabilizing or destabilizing influences.
Much is known about the regulatory processes involving system parameters that stabilize cortisol rhythmicity on the cellular/molecular level. We know much less about parametric influences operating on other levels of scale, including at the cognitive level of thought and perception, individual behavior, social behavior, or community and political behavior.

Objective: The objective is to investigate adaptive (proadaptive and maladaptive) response to significant stress, both acute and chronic, as might be experienced during human spaceflight.



Impact: it informs development of novel patient care strategies, benefiting Super-utilizers as well as addressing the significant challenge their care poses within the healthcare system.

Deliverables: specific recommendations for developing a resilience and recovery model appropriate to the challenges of spaceflight, which reflects a high-level integrative approach to human adaptation in the face of chronic stress and the potential for traumatic experience.

Approach:

- This investigation is ground-based (no space flight testing)
- The approach is based on the classic observation that human adaptive response is modulated by influences operating on multiple levels of scale, from autonomic through cognitive, behavioral, and social.
- Specifically, this effort builds on existing research that describes how these influences synergistically act on the HPA-axis (the brain's stress/relaxation center) to:
  - (a) mediate changes in the amplitude and frequency of pulsatility for stress and relaxation hormones, including cortisol and beta-endorphin; where
  - (b) the resulting rhythmicity is observed to display nonlinear properties that feed back to adaptive response on multiple levels of scale; and, where
  - (c) resulting feedback loops exhibit both positive (chaotic) and negative (inhibitory) characteristics that function as key drivers of health and adaptive behavior

Proposed Funding:	*Year 1*	*Year 2*	***Total***
	$400K	$400K	**$800K**

<u>Project Plan</u>

1: HPA-axis model development and test (Y1)
2: develop ACE assessment and resilience strategies (Y2)
3: recommendations based on testing on cohorts

POC Contact Information: Lee Berk (LLU)
Phone: 909-213-7341 Email: lberk@llu.edu

What we know about stress

- Human stress response originates in the Hypothalamic-Pituitary-Adrenal (HPA) axis.
- For humans the need to maintain HPA-axis stability is supported by successive layers of feedback systems that can exert complementary stabilizing influences.
- Much is known about the regulatory processes involving system parameters that stabilize cortisol rhythmicity on the cellular/molecular level.
- We know less about parametric influences operating on other levels of scale, including at the cognitive level of thought and perception, individual behavior, social behavior, or community and political behavior.
- Astronaut Scott Kelly's epigenetic DNA expression has changed by 7% due to his year-long stay in the international Space Station, and significant attention is being given to DNA methylation as a health consideration related to space flight.
- Methylation of DNA in the HPA-Axis is responsible for increased stress reactivity and chronic activation of immune inflammatory response, which is known to significantly contribute to early onset of chronic diseases and early death.

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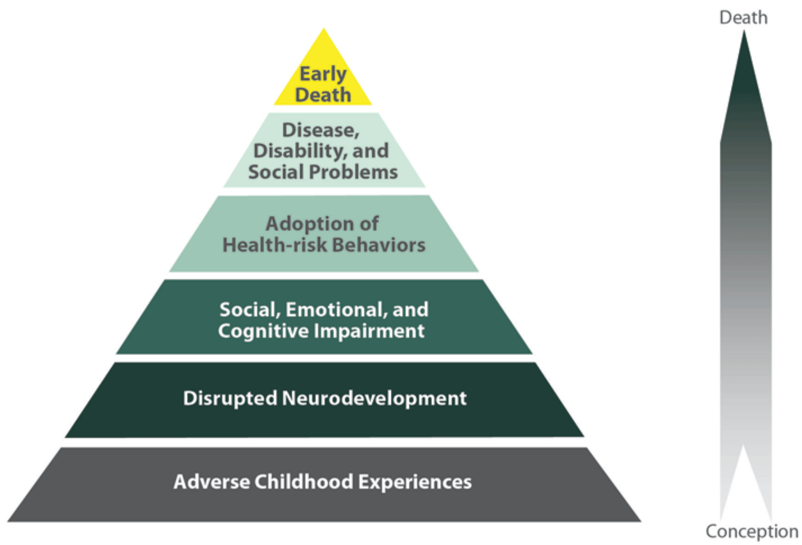
Summary of multiscale stability factors in HPA-Axis in humans

Layers of Influence	Regulatory Process (Rule Sets that drive self-organization)	Pathology	Agency	Maintaining & Restoring Stability
Molecular (Intrinsic)	Genetic	HPA-axis instability via cortisol and beta-endorphin rhythmicity,	Epi-genetics- Methylation, Etc.	Pharmacological Agent(s)
Cellular (Intrinsic)	Immune System, Hormonal Operations, Etc.	Various Disease states: • Inflammatory Process, • Cell Injury & Death,	Physiological Systems	Physical Medicine
Cognitive (Extrinsic)	Rationality (Logic)	Cognitive Distortions, Mental Illness	Neurological Systems	Behavioral Medicine, Mental Health Therapist,
Behavioral (Extrinsic)	Core Values, Personal Code	Lack of Self-control Impulsivity, Stress Reactivity	Individuals	Self + Resources Below
Family (Extrinsic)	Oral & Written Rules, Family Traditions	Divorce, Abandonment, Juvenile Delinquency	Family Systems	Parents, Grand Parents, Relatives
Social (Extrinsic)	Social Conventions, Manners & Respect, Ethics	Incivility, Discourtesy, Bullying	Friends, Social Groups,	Peer Pressure, Group Influence
Community (Extrinsic)	Contracts & Agreements Corporate Governance, Policy & Regulations,	Poverty, Ignorance, Inequity	Business and Commerce, Coalitions, Cooperatives	Civil Law Systems, Schools, Churches,
City, County, State, Federal (Extrinsic)	Charters & Constitutions, Codes, Ordinances, & Laws	Violations of Law, Crime	Governments via Law Enforcement,	Criminal Law via Justice system
Geo-Political (Extrinsic)	Treaties, International Law,	Conflict & Hostilities, War,	Nation States via Militaries,	United Nations International Law Court, Tribunals

Connection between cortisol rhythmicity and health care

- Vincent Felitti's, M.D., pioneering work in the now famous ACE Study, which explores the impact of trauma during childhood has resulted in assessment tools and predictive models for a wide variety of health and behavioral outcomes related to early-life toxic stress and trauma.

- These models point to neurological changes that are now understood to reflect the results of DNA methylation on set point in the HPA-Axis, the stress center of the brain.



Mechanism by Which Adverse Childhood Experiences Influence Health and Well-being Throughout the Lifespan

ACE Study – CDC-Kaiser – 17,000 patients - http://www.cdc.gov/violenceprevention/acestudy/about.html

There is a critical need for a computer model of the cortisol cycle in the HPA-axis to understand stress response across scales

- Cortisol rhythmicity displays identifiable nonlinear properties, which suggests the operation of a nonlinear system
- Effective regulation is important to keep the rhythm stable
- It is important to develop a better understanding of how all of the above works because a lot of cost to healthcare and society is riding on our ability to develop solutions.
- Multiscale modeling and simulation of cortisol rhythmicity can be accomplished by nonlinear dynamical system techniques.
- These strategies involve the use of powerful mathematical tools and related concepts that JPL applies to space flight and high-level engineering problems. Also, nonlinear systems can be modeled in a computer, allowing us to study how they work.

Collaborating Institutions and Partners

- Jet Propulsion Laboratory – California Institute of Technology (JPL)
- Loma Linda University (LLU)
- Adventist Health Glendale (AHGL)
- California Institute of Preventive Medicine (Vincent Felitti)
- UCLA Cousins Center for Psychoneuroimmunology, (Steve Cole)
- Duke University Center for Spirituality, Theology and Health (Harold Koenig)

Specific Aims

- Evaluate the ACE Score model as a screening resource for prospective astronauts and expand application of basic concepts to develop assessment tools for adult-experienced trauma such as might occur during space missions.

- Develop/adapt mathematical and computer models that describe the effects of stress and trauma on circadian and ultradian rhythmicity in the HPA-Axis, including attractor-state instabilities and pathways for resilience that may result from multi-layered parametric influences.

- Propose a prevention, resilience, and recovery paradigm that builds on insights gained from studying centenarians in the Blue Zone longevity project at Loma Linda University, especially those who have high ACE Scores and have enjoyed good health, nonetheless.

Cohorts

- Three cohorts will be identified.
- Two cohorts will be recruited from among the approximately 4000 super-utilizers (patients with complex-care needs who are frequently seen in the emergency department or admitted to the hospital and who appear to display toxic stress or trauma-related behavior and health outcomes as predicted by the ACE-Score algorithm) that have been identified at Adventist Health Glendale.
- The first of these cohorts will be super-utilizers with high ACE Scores.
- The second cohort will include adults whose precipitating toxic stress or trauma occurred in adulthood.
- The third cohort will include subjects of great longevity currently being studied in the Blue-Zone project at Loma Linda University.

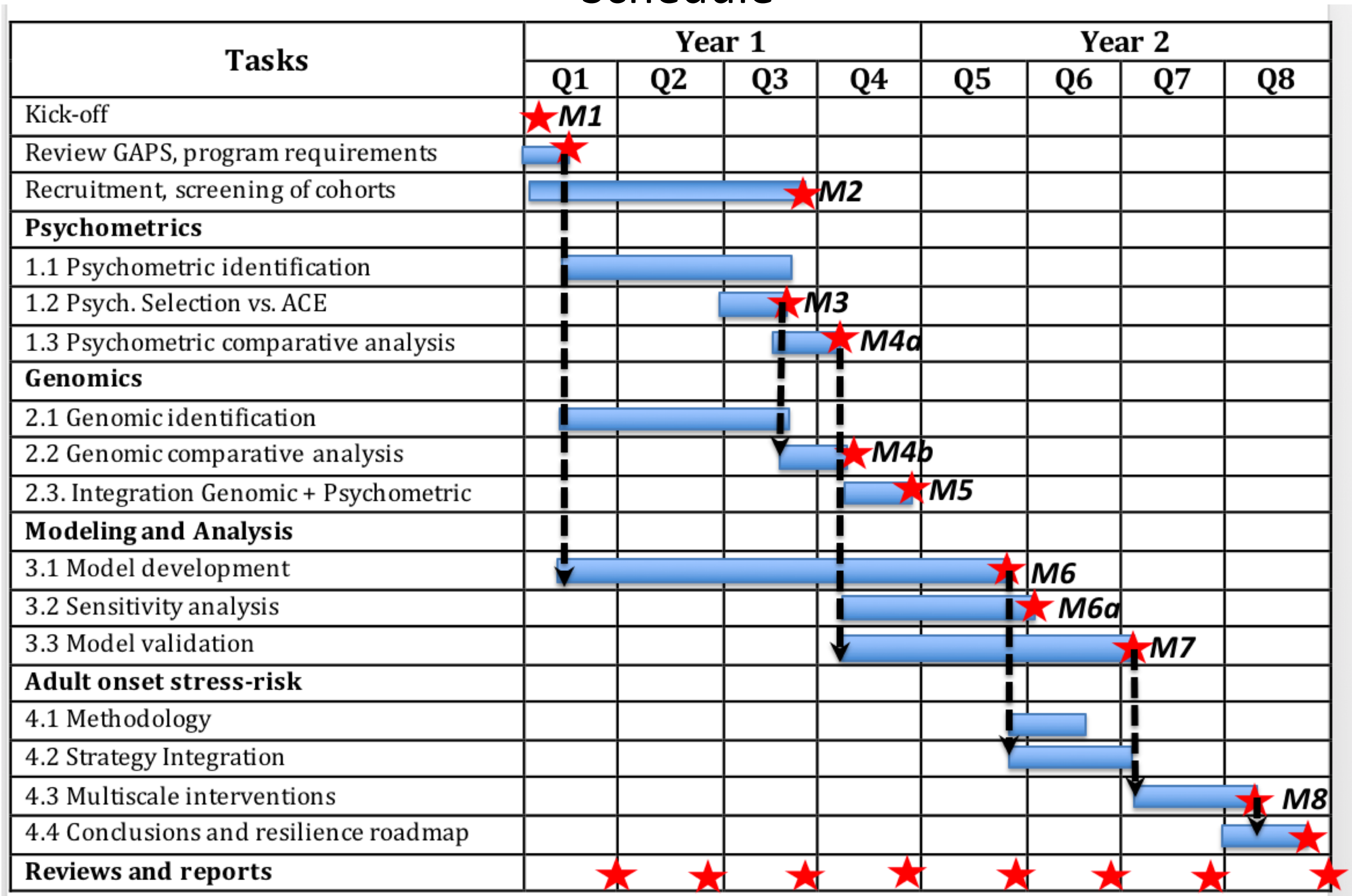
Jet Propulsion Laboratory
California Institute of Technology

Task List

Task List: Producing a state-of-the-art methodology and associated tools for reducing cognitive/behavioral impairment and improving health outcomes during space-flight.

Psychometrics	Genomics	Multiscale Analysis	Adult-onset Stress Risk
Task 1. *Identify relevant cognitive/behavioral traits of Blue Zone (long-lived) vs. Super-utilizer cohorts*	**Task 2** *Identify relevant neuro-pathways and mediators (immune, endocrine, corticotropic & dopaminergic, etc.)*	**Task 3** *Develop nonlinear mathematical model and computer simulations of stress effects across scales*	**Task 4** *Develop methodology and bio/psychometric tools for assessing and mitigating adult-onset stress risk (spaceflight)*
Task 1.1 Identify the high-ACE cohort vs. the adult-onset stress-risk cohort among Super-utilizers	**Task 2.1** Conduct comparative statistical analysis of genomic data for the three cohorts	**Task 3.1** Conduct sensitivity analysis	**Task 4.1** Integrate outputs from Psychometric, Genomic and Multiscale Analysis into strategy design
Task 1.2 Conduct comparative statistical analysis of psychometric data for the three cohorts	**Task 2.2** Conduct integrative analysis correlating genomics and psychometrics	**Task 3.2** Correlate simulations with psychometric and neuro-physiological data/trajectories	**Task 4.2** Explore interventions for each level of scale (molecular, cognitive, behavioral, social)
Task 1.3 **Outcome:** Detail the stress-effect implications from comparison/contrast between the three cohorts	**Task 2.3** **Outcome:** Construct stress-effect neuro-physiological model (exploring implications for causal links)	**Task 3.3** **Outcome:** Produce nonlinear multiscale framework to predictively simulate trajectories for neuro-physiological & cognitive/behavioral stress effects	**Task 4.3** **Outcome/Deliverables:** Produce state-of-the-art strategies to reduce the effects of chronic stress & to promote recovery from potentially traumatic experiences
		Feedback Validation	

Schedule


Tasks
Year 1
Year 2
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Kick-off
Review GAPS, program requirements
Recruitment, screening of cohorts
Psychometrics
1.1 Psychometric identification
1.2 Psych. Selection vs. ACE
1.3 Psychometric comparative analysis
Genomics
2.1 Genomic identification
2.2 Genomic comparative analysis
2.3. Integration Genomic + Psychometric
Modeling and Analysis
3.1 Model development
3.2 Sensitivity analysis
3.3 Model validation
Adult onset stress-risk
4.1 Methodology
4.2 Strategy Integration
4.3 Multiscale interventions
4.4 Conclusions and resilience roadmap
Reviews and reports
M1
M2
M3
M4a
M4b
M5
M6
M6a
M7
M8