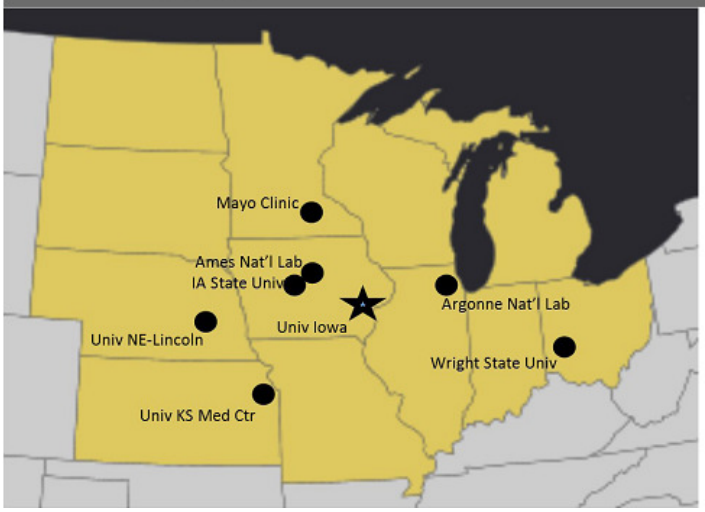
MIDWEST POSTDOCTORAL SYMPOSIUM



Friday, May 2, 2014

9 am to 4:30 pm

College of Public Health Building
University of Iowa
Iowa City, Iowa

Sponsors: Office of the Vice President for Research, Graduate College, College of Medicine, College of Public Health, IIHR-Hydroscience and Engineering, College of Engineering, and UIPDA.

Midwest Postdoctoral Symposium 2014

Program:

8:30 – 9:15 Registration/Breakfast (C217)

9:15 – 9:30 Welcome and Opening (N120)

9:30 – 10:00 **Keynote:** 'Comparing employment in academia and industry' (N120)

Dan Reed, Vice President for Research and Economic Development, University of Iowa

10:00 – 10:30 Media promotion and handling media research inquiries (N120)

Richard Lewis, Senior Research Writer and Editor for the Office of Communication and Marketing, University of Iowa

10:30 – 11:30 Posters/Networking (Atrium)

11:30 – 12:30 Intellectual Property and Panel discussion on business ventures (N120)

David Conrad, Deputy Director of Economic Development in the Office of the Vice President for Research and Economic Development, University of Iowa

Paul Dymerski, Associate Director of New Ventures & IP Assessment, University of Iowa Research Foundation

Paul Heath, Director of Small Business Development Center, University of Iowa

12:30 – 1:30 Lunch (Atrium)

1:30 – 2:30 Panel discussion on starting as new faculty (N120)

Ryan Carnahan, Clinical Associate Professor of Epidemiology, University of Iowa

Craig Just, Assistant Professor of Civil and Environmental Engineering, University of Iowa

Catherine Musselman, Assistant Professor of Biochemistry, University of Iowa

Rajan Sah, Assistant Professor of Internal Medicine and Cardiology, University of Iowa

Sarit Smolikove, Assistant Professor of Biology, University of Iowa

2:30 – 3:30 Posters/Networking (Atrium)

3:30 – 4:30 Postdoctoral research presentations (N120)

3:30-3:50 – 'Transdifferentiation off Bone Marrow-Derived Stem Cells into Schwann-like Cells on Micropatterned Polymer Substrates for Peripheral Nerve Regeneration Strategies'

Svitlana Zbarska, Genetics, Development and Cell Biology, Iowa State University

3:50-4:10 – 'Isolation and analysis of Ngn3/CD133+ Endocrine Precursor Cells From Human Exocrine Tissue'

James McGarrigle, Transplant/Surgery, University of Illinois at Chicago

4:10-4:30 – 'Identification of a lysozyme receptor and a new class of lysozyme inhibitors in Gram-positive bacteria'

Kyle Williams, Microbiology, University of Iowa

4:30 Awards/Closing (N120)

Poster Presentation Locations

Poster/networking sessions will be held in the Atrium of the Public Health Building. Session 1 posters (10:30 – 11:30) should be set up between 8:30 – 10:30 and removed by 12:30. Session 2 posters (2:30 – 3:30) should be set up between 12: 30 – 2:30 and removed by the end of the day.

Name	Title	Poster Number	Session
Bai, Zhenhua	Single-band red upconversion luminescence from morphology and size controllable Er^{3+}/Yb^{3+} doped MnF_2nanostructures	2	10:30 - 11:30
Bai, Zhenhua	On-Chip Development of Hydrogel Microfibers from Round to Square/Ribbon Shape	22	2:30 - 3:30
Bogunovic, Hrvoje	Mosaicing and Multi-Field Layer Segmentation of 3-D Retinal OCT	38	2:30 - 3:30
Brandes, Elke	Growing switchgrass on a sub-field scale could increase farmers' profits in Iowa	26	2:30 - 3:30
Brenza, Timothy	Size and Chemistry Affect Cellular Distribution after Intranasal Administration of Nanoparticles	36	2:30 - 3:30
Caulfield, Maggie	Granulocytes are Early Effectors in Neuromyelitis Optica	5	10:30 - 11:30
Chadda, Rahul	Reversible Dimerization of a Cl-/H+ Antiporter: A model for Membrane Protein Folding	33	2:30 - 3:30
Chikka, Madhusudana	Role of p38MAPK in alpha-synuclein induced cell non-autonomous susceptibility to oxidative stress.	6	10:30 - 11:30
Choi, Jiwoong	Serial CT Based Assessment of Regional Lung Function Changes in Cancer Patients	14	10:30 - 11:30

Das, Satyabrata	Alternate promoter usage contributes to Nanog autoregulation by a multilayered mechanism	9	10:30 - 11:30
Gander, Phillip	Midwest Postdoctoral Forum (MWPDF), an excellent model for a regional collaboration among postdoctoral communities	21	all day
Gill, Gurman	An Automated Initialization System for Robust Model-Based Segmentation of Lungs in CT Data	15	10:30 - 11:30
Grewal, Jasreen	Optimizing ethanol production in integrated corn/soybean biorefineries	30	2:30 - 3:30
Grinnage-Pulley, Tara	Trimannose oligosaccharides promote pro-inflammatory response and lesion resolution during *Leishmania major* infection	20	10:30 - 11:30
Guo, Jiannan	The Myc mystery: sequence specificity vs genome-wide occupancy	10	10:30 - 11:30
Guo, Jiannan	Regulation of RNA Polymerase II Termination by Phosphorylation of Gdown1	34	2:30 - 3:30
Hamann, Cara	Pedal Portal: A naturalistic study of child bicyclist behaviors and risk exposure	32	2:30 - 3:30
Hing, Benjamin	A Genome-Wide Targeted Capture Approach for DNA Methylation Study	35	2:30 - 3:30
Jaishy, Bharat	Lipid-overload impairs lysosomal enzyme activity and autophagosome turnover by inducing Protein kinase C (PKC)-NADPH oxidase 2 (NOX2) Pathway	11	10:30 - 11:30
Khanchi, Amit	Influence of weather and swath density on drying rate potential of corn stover	29	2:30 - 3:30
Kolb, Ryan	Metformin, inflammasome activation and the IL-1/IL1R1 axis in obesity associated breast cancer progression.	17	10:30 - 11:30
Lampert, David	Integrating Dynamically-Downscaled Climate Simulations into an Iowa Watershed Model for Forecasting Climate Change Impacts on Water	27	2:30 - 3:30

Markan, Kathleen	Targeting Endogenous FGF21 Activity to Enhance Insulin Sensitivity	13	10:30 - 11:30
Markutsya, Sergiy	New Approaches in Mesoscale Modeling	23	2:30 - 3:30
McGarrigle, James	Isolation and Analysis of Ngn3/CD133+ Endocrine Precursor Cells From Human Exocrine Tissue	12	10:30 - 11:30
Mudunkotuwa, Imali	Engineered Nanomaterials in Aqueous Environments: Interactions, Transformations and Implications	24	2:30 - 3:30
Nenadic, Ivan	Measuring Mechanical Properties of the Pancreas in Vivo	18	10:30 - 11:30
Parker, Krystal	Medial frontal D1 dopamine signaling is required for low-frequency oscillations and ramping neural activity during interval timing	7	10:30 - 11:30
Ponou, Simeon	Rational Synthesis of Zintl Phases: A still challenging Task	3	10:30 - 11:30
Rajewski, Daniel	Wind farm wake detection from surface measurements during the 2013 Crop Wind-energy Experiments (CWEX-13)	28	2:30 - 3:30
Rashid, Adnan	Reproducibility of Total Retinal Thickness in 5 SD-OCT Scanners using Iowa Reference Algorithm	37	2:30 - 3:30
Safayi, Sina	Midwest Postdoctoral Forum (MDWPDF), an excellent model for a regional collaboration among postdoctoral communities	1	all day
Sharma, Bhavna	Evaluation of algal biofuel production potential using Geographic Information Systems: A review	31	2:30 - 3:30
Singh, Brajesh	Role of human nectin-4 and F-actin in cell-to-cell spread of measles virus in airway epithelial cells	19	10:30 - 11:30
Tandon, Manish	Runx2 exerts differential response in growth factors- or hormone-induced signaling in normal or metastatic breast cancer models.	16	10:30 - 11:30

Umesalma, Shaikamjad	Deficiency of C-Jun-N-Terminal Kinase Prevents Angiotensin II-Induced Inward Remodeling but Not Hypertrophy in Cerebral Arterioles	39	2:30 – 3:30
White, Paul	Plant Cell Wall Structure and Hydration Investigated by Sensitivity-Enhanced Solid-State NMR	25	2:30 - 3:30
Wilson, Seth	Molecular dynamics study of correlation between bulk and solid-liquid interface properties in pure metals	4	10:30 - 11:30
Zbarska, Svitlana	Transdifferentiation off Bone Marrow-Derived Stem Cells into Schwann-like cells on Micropatterned Polymer Substrates for Peripheral Nerve Regeneration Strategies	8	10:30 - 11:30

Single-band red upconversion luminescence from morphology and size controllable Er^{3+}/Yb^{3+} doped MnF_2 nanostructures

Zhenhua Bai[1], Reza Montazami[1], Nastaran Hashemi[1]

[1]Department of Mechanical Engineering, Iowa State University

Abstract

MnF_2 nanostructures have been prepared via a solvothermal method. The morphology of the nanocrystals could be controlled from nanoparticle to nanocluster and nanolantern. Single-band red upconversion emission can be generated in Er^{3+}/Yb^{3+} codoped MnF_2 nanoclusters.

On-Chip Development of Hydrogel Microfibers from Round to Square/Ribbon Shape

Zhenhua Bai[1], Reza Montazami[1], Nastaran Hashemi[1]

[1]Department of Mechanical Engineering, Iowa State University

Abstact

The gelatin fibers with controlled size and shape are fabricated by microfluidic device. The cross section can be tuned from round to square/ribbon by controlling the experiment parameters. The experiment results fit well with the COMSOL simulation results in terms of shape evolution.

Mosaicing and Multi-Field Layer Segmentation of 3-D Retinal OCT

Hrvoje Bogunovic[1], Michael D. Abramoff, Xiaodong Wu, Pavlina Kemp, Mona Garvin, Wallace L.M. Alward, John H. Fingert, Young Kwon, Milan Sonka

[1]Electrical and Computer Engineering, University of Iowa

Abstract

Purpose: First, to increase the retinal OCT coverage by creating a mosaic of OCT images from multiple spatially overlapping fields. Second, to perform a multi-field co-segmentation of intraretinal layers, assuring consistent segmentation of the fields in the overlapped areas. Methods: A 9-field per eye acquisition was performed where a subject fixates on 9 spots in a 3×3 grid pattern. Subjects were imaged with spectral domain OCT Spectralis. In addition, the device acquires 2D SLO fundus, co-registered with the OCT image. We create a mosaic by performing 2D en-face, affine alignment of the imaged fields, based on matched Speeded Up Robust Features keypoints. For the alignment, the SLO images are used as surrogate to projection OCT images due to their higher spatial resolution and pronounced texture. This is followed by the graph-search based multi-field co-segmentation of intraretinal layers. All 9 fields are segmented simultaneously, imposing a priori soft intrasurface-interfield constraint for each pair of overlapping fields Results: Our method was evaluated on acquisitions from 10 glaucoma patients. Qualitatively, the obtained thickness maps show no stitching artifacts, compared to pronounced stitches when the fields are segmented independently. Quantitatively, two ophthalmologists manually traced ILM, RNFL, GCL+IPL, and RPE layers. The average unsigned error of the automated method was comparable to the average difference between the observers. Conclusions: Building a mosaic of multiple fields is an effective approach for increasing the coverage of imaged retina. As opposed to segmenting layers in each of the fields independently (the current state of the art), the proposed co-segmentation method obtains consistent segmentation results across the overlapped and registered areas, producing accurate and artifact-free thickness maps.

Growing switchgrass on a sub-field scale could increase farmers' profits in Iowa

Elke Brandes[1], David Muth[2], Ian Bonner[3,4], Kara Cafferty[3,4], Lisa Schulte-Moore[5], Emily Heaton[1]

[1]Agronomy, Iowa State University

[2]AgSolver, Inc.

[3]US-Department of Energy

[4]Idaho National Laboratory Department of Biofuels & Renewable Energy Technologies

[5]Natural Resource Ecology and Management, Iowa State University

Abstract

The USA has a large potential to reduce carbon emissions and increase community resilience by scaling up renewable energy production. A promising new energy source is lignocellulosic biomass from dedicated perennial crops, often referred to as second generation (2G) biomass. Despite of numerous advantages, 2G biomass production and utilization lags behind mandates. Currently, farmers have little incentive to change management from grain crops to lignocellulosic energy feedstock. Recent crop budget calculations for perennial grasses such as switchgrass resulted in high breakeven prices that are unlikely to be economically feasible without subsidies. However, the underlying economy changes when subfield spatial variation of soil characteristics and associated corn yield variability is taken into account. We applied a modeling framework that integrates agronomic computing tools to analyze the business case for integrated agricultural landscape management in Iowa. Current corn yields associated with soil properties were mapped to agricultural land. Crop budgets were used to assess subfield profitability for corn. Three scenarios of management change to switchgrass production on target areas unprofitable for corn were simulated, assuming high, low or medium yields. First results revealed high yield variation on a sub-field resolution. We could show that Iowa farmers lose money with corn on a considerable percentage of land, even if average yields per field seem adequate. The integration of switchgrass into the agricultural landscape could allow spatial intensification in combination with an economic benefit for the farmers and the potential to boost the local bioenergy economy.

Size and Chemistry Affect Cellular Distribution after Intranasal Administration of Nanoparticles

Timothy M. Brenza[1], Latrisha Petersen, Yanjie Zhang, Lucas Huntimer, Amanda Ramer-Tait, Michael J. Wannemuehler, Balaji Narasimhan

[1]Chemical and Biological Engineering

Abstact

Size and route of administration have been shown to greatly impact the biodistribution and bioavailability of biodegradable particles. For respiratory infections, intranasal administration offers many advantages, including ease of administration, induction of mucosal immunity, and reduced systemic exposure due to the localization of the delivery vehicle within the target organ. These same properties, i.e., size and route, along with particle chemistry have been shown to influence particle uptake by antigen presenting cells (APCs), which is an essential first step in the induction of an adaptive immune response for vaccines or as the first line of defense against exogenous particles. For particle size comparative studies, many researchers utilize non-degradable particles. In this work, the synthesis of monodisperse biodegradable polyanhydride particles of multiple sizes has enabled the quantitative evaluation of the role of particle size and chemistry upon cellular distribution after intranasal administration.

Granulocytes are Early Effectors in Neuromyelitis Optica

Maggie Caulfield[1], Tanya Kaptzan[1], Reghann LaFrance-Corey[1], Charles Howe[1], Claudia Lucchinetti[1]

[1]Neurology, Mayo Clinic

Abstract

Neuromyelitis optica (NMO) is a CNS inflammatory disorder in which astrocytes are selectively targeted through the binding of a pathogenic, complement-activating IgG autoantibody (NMO-IgG) to the ectodomain of aquaporin-4 (AQP4). AQP4 is the principal CNS water channel where it is expressed on astrocytic foot processes at astro-endothelial, astro-pial, and astro-neuronal synapses. Detection of the NMO-IgG autoantibody in serum unifies a growing spectrum of clinical disorders known as NMO spectrum disorders (NMOSD), which include optic neuritis, transverse myelitis, intractable vomiting and hiccups, dysphagia, inappropriate anti-diuresis, central hypotension, oculomotor dysfunction, hearing loss, narcolepsy, central endocrinopathies, posterior reversible encephalopathy, and generalized encephalopathy. Our observations in NMO tissues demonstrate that the disease is a *global astrocytopathy* including evidence of an early and robust astrocytic stress response, frequently within regions of tissue not associated with overt demyelination. We also find eosinophils and other granulocytes near reactive astrocytes, in the absence of complement deposition, suggesting that these cells have been recruited to the CNS parenchyma through a distinct mechanism. Upon activation, astrocytes can synthesize many immunomodulatory and immunopathogenic cytokines and chemokines. Therefore, we hypothesize that astrocytes orchestrate early granulocytic recruitment to the CNS in NMO. Using primary murine astrocyte cultures we have found that stimulation with NMO-IgG drives a robust pro-inflammatory, pro-granulocytic response at the transcript level via microarray analysis, as well as the release of large amounts of the granulocytic chemokines CCL5, CXCL1, and CXCL2. Further, *in vivo* granulocytes rapidly accumulate in the brain following intracranial NMO-IgG injection. Although the consequences of early granulocyte infiltration in NMO are largely unknown, we hypothesize that astrocytes act at the nexus of brain-immune interactions to coordinate this trafficking. Further, we believe that granulocytes are obligate effectors in NMO tissue and represent a novel and powerful target for therapeutic intervention, likely before irreversible tissue destruction has occurred.

Reversible Dimerization of a Cl-/H+ Antiporter: A model for Membrane Protein Folding

Rahul Chadda[1], Venky Krishnamani, Kacey Mersch, Janice L. Robertson

[1]Biophysics and Molecular Physiology, University of Iowa

Abstract

How does a greasy protein surface find its greasy protein partner in the greasy lipid bilayer to fold faithfully into its native structure? This is a question that is central to membrane protein folding - a field whose growth has been limited by a simple lack of model systems. Recently, we designed a stable and functional monomeric form of the normally homodimeric Cl-/H+ antiporter ClC-ec1, and studies show that the protein can be shifted back to the dimer state with mutations and in certain lipid conditions. We are now studying this reversible dimerization as a model to study membrane protein folding, acknowledging that the same physical forces driving dimerization operate in the more complicated, experimentally inaccessible folding landscape. To measure the energy of association in membranes, the monomer/dimer populations are quantified using Förster resonance energy transfer in the dimer state and single-molecule microscopy to count photo-bleaching of subunits. Using ClC-ec1, we will investigate two alternative hypotheses that have pervaded discourse in this field: (i) transmembrane helix interactions are enthalpy- driven by van der Waals forces at complementary surfaces and (ii) association is driven by the gain in lipid entropy upon helix association. Here, we have a unique ability not available in soluble protein folding work - to change the solvent: the lipids. These results will provide insight into the driving forces for membrane protein interactions, and will provide a foundation for attacking questions underlying protein folding in the strange solvent that is the lipid bilayer

Role of p38MAPK in alpha-synuclein induced cell non-autonomous susceptibility to oxidative stress

Madhusudana Rao Chikka[1], Rob Todd[1], Marcus Tatum[1], Veena Prahlad[1]

[1]Biology, University of Iowa

Abstract

Degenerative diseases caused by disruption of protein homeostasis typically result in selective vulnerability of a subset of cells even though the protein in question is more widely expressed. For instance, in cases of Familial Parkinson's Disease the protein α-synuclein which is central to the death of dopaminergic neurons of the Substantia Nigra is expressed not only in dopaminergic neurons themselves, but also in other neuronal and non-neuronal tissues including skin fibroblasts. Thus, the selective neuronal vulnerability that occurs upon the misregulation, or mutation, of a widely expressed protein remains to be understood.

We have utilized C. elegans as a model system to ask whether cell non-autonomous mechanisms can be responsible for the selective vulnerability of dopaminergic neurons upon the aberrant expression of α-synuclein. Consistent with previous observations, the expression of α-synuclein in muscle cells of C. elegans caused progressive cellular dysfunction, tissue damage and paralysis. Also α-synuclein expression increased susceptibility of the organism to oxidative stressors, as well as increased dopaminergic neuron loss upon treatment with neurotoxic Rotenone. As previously seen in mammalian systems, α-synuclein expression causes an increase in oxidative damage as assessed by increased protein carbonylation groups. However, one of the key protective responses to oxidative damage i.e. the activation of the NRF-2/SKN-1 does not occur. We find that this may be due to the systemic, cell non-autonomous down regulation of p38 Mitogen Activated Protein Kinase (p38 MAPK) signaling pathway throughout the organism. p38 MAPK signaling in C. elegans is a key pathway required for the organism to adequately respond to oxidative stress, and expression of p38MAPK in intestinal cells can rescue the organismal susceptibility to oxidative stress and neuronal loss due to neurotoxic compounds. We are currently investigating the mechanisms by which a-synuclein causes p38 MAPK dysregulation.

Serial CT Based Assessment of Regional Lung Function Changes in Cancer Patients

Jiwoong Choi[1,2,3], Ching-Long Lin, John D. Newell Jr., Mohammed M. Milhem, Tina Knutson, Jean Tessier, Eric A. Hoffman

[1]Mechanical Engineering, University of Iowa

[2]IIHR—Hydroscience and Engineering, University of Iowa

[3]Advanced Pulmonary Physiomic Imaging Laboratory, University of Iowa

Abstract

RATIONALE: Extra-thoracic tumors send out pilot cells that attach to the pulmonary endothelium. This could alter regional lung mechanics, and the process may precede CT evidence of metastatic pulmonary nodules. We seek to develop a method to measure small scale lung biomechanics using CT imaging and CT image matching technologies, and to assess the biomechanical signals in cancer subjects in comparison with controls. **METHOD:** We retrospectively selected temporally-spaced inspiratory CT scans of 18 cancer (sarcoma) patients (9 showed lung metastases at distal time points), and two control groups: 7 normal non-smokers and 12 asymptomatic smokers. We performed image registration for local-to-local matching of selected pairs per subject, and derived local structural and functional changes. We compared local contributions to the global lung volume over time to detect regional hypo-expansion or hyper-expansion (HE), and measured tissue volume change in HE regions. Welch two sample t test was used for comparison between groups. **RESULTS:** Regions in the lung of cancer patients were found undergoing a large local expansion in time. Sub-sets of these HE lung regions were associated with metastatic lesions but extended beyond the lesion and in contra-lateral lung in some patients. HE was minimal in the non-smokers, slightly elevated in the normal smokers, and significantly ($p < 0.05$) elevated in the over-all sarcoma group. In association with HE, over-all lung tissue (non-air) volume was significantly increased ($p < 0.0003$). “Tissue” volume increase may represent regional inflammatory processes. **CONCLUSION:** The method developed and validated in control subjects can detect temporally related regional structural and functional changes such as HE and inflammation at a sub-acinar scale in the lung of cancer patients. This method may provide a diagnostic and prognostic means to objectively characterize regional responses in the lung following oncological treatment and CT monitoring for lung metastases.

Alternate promoter usage contributes to Nanog autoregulation by a multilayered mechanism

Satyabrata Das[1], Snehalata Jena[1], Dana N. Levasseur[1]

[1]Internal Medicine, University of Iowa

Abstract

Among the core pluripotency transcription factor triad of Nanog, Oct4 and Sox2, Nanog remains functionally unique owing to its ability to repress genes that specify all three germ layers as well as the extraembryonic primitive endoderm genes. The expression of Nanog remains heterogeneous in the embryonic stem cells (ESCs) and transient downregulation in a subset of cells directs them toward differentiation. How the levels of Nanog, which are tightly regulated in ESCs, are dampened to commit to lineage specification remains unclear. We had recently reported a novel upstream alternate Nanog promoter (P2) by investigating the cryptic RNAs originating from the annotated *Nanog* gene enhancer. Here we report that several different transcripts originate from P2 by alternative splicing. Open chromatin structure and transcription machinery enrichment at P2 keeps it active in differentiated and adult tissues. Full length P2 transcripts were cloned from brain, lungs and bone marrow where the enrichment of isoforms points to a tissue specific pattern. The Nanog protein levels from the P2 transcripts are stably repressed by the presence of long and multiple upstream open reading frames (uORFs) or by encoding protein variants with much shorter half-life. Most importantly, downregulation of the P2 transcripts leads to a slight slowdown in the ESC growth, but differentiation is delayed as observed by reduced embryoid body size and delayed persistence of pluripotency markers as well as a reduced upregulation of differentiation markers. Moreover, downregulation of P2 transcripts also compromised reprogramming of fibroblasts by generating fewer iPS colonies. Our results suggest that Nanog expression is modulated by two independent promoters and Nanog levels are maintained by a complex multi-layered regulation.

Midwest Postdoctoral Forum (MWPDF), an excellent model for a regional collaboration among postdoctoral communities

P.E. Gander[1]

[1]Neurosurgery, University of Iowa

Abstract

Due to the scarcity of networking among regional postdoctoral communities, the Midwest Postdoctoral Forum (MWPDF) was formed in 2012. The forum was created to: 1) bring individual postdoctoral communities and perspectives together to form a platform for efficient and innovative regional cooperation; and 2) promote communication among regional postdoctoral communities by facilitating collaboration in social and professional areas.

The MWPDF has been used as a platform to share: 1) experiences, *i.e.* adapting successfully implemented policies used by individual members at other member institutes; 2) information, *i.e.* circulating announcements regarding local/regional events; and 3) resources, *i.e.* opening local events to postdoctoral communities from member institutions.

The MWPDF is currently made up of eight institutions from Iowa, Illinois, Kansas, Minnesota, Nebraska and Ohio, one of which is the University of Iowa. This year's Midwest Postdoctoral Symposium hosted by the University of Iowa is the first meeting affiliated with the MWPDF. We hope in the years to come that the annual symposium will travel to other institutions involved in the MWPDF and become a *truly* regional event.

An Automated Initialization System for Robust Model-Based Segmentation of Lungs in CT Data

Gurman Gill[1], Matthew Toews[2], Reinhard R. Beichel[3]

[1]Dept. of Electrical and Computer Engineering and The Iowa Institute for Biomedical Imaging, The University of Iowa

[2]Brigham and Women's Hospital, Harvard Medical School

[3]Dept. of ECE and Dept. of Internal Medicine and The Iowa Institute for Biomedical Imaging, The University of Iowa

Abstract

Lung segmentation methods are required for automated lung image analysis and to facilitate tasks like lung volume calculation and quantification of lung diseases. Model-based techniques, such as Active Shape Models (ASM) have been employed for segmenting lungs because they incorporate prior knowledge of anatomical shape variation into the segmentation process. However, they suffer from the drawback that the model must be initialized sufficiently close to the target. We propose a novel approach for initializing ASMs based on predicting three landmark points (left lung apex, right lung apex and carina) using a feature-based alignment (FBA) method. These landmark points are subsequently used to calculate initial model parameters. The approach was evaluated on a diverse set of 98 CT scans of normal and diseased lungs by comparison to an independent reference standard. For segmentation results based on the new initialization approach, the mean and standard deviation of the Dice coefficient was 0.976 +/- 0.025. In comparison, the Dice coefficient of lung segmentations based on the previously utilized initialization method was 0.971 +\- 0.040. The new RASM initialization approach is 3-times faster than the previously utilized method and can be expanded by including additional landmarks. Keywords: Lung segmentation, computed tomography (CT), model initialization

Optimizing ethanol production in integrated corn/soybean biorefineries

J. Grewal[1], J.K. Sekhon[1], L. Yao[1], L. Johnson[1], T. Wang[1], K. Rosentrater[1], S. Jung[1]

[1]Food Science and Human Nutrition, Department of Food Science

Abstract

Today, most fuel ethanol production is achieved by dry-grind processes by using corn grain. Thus, more than 10% of the 150 billion gal of annual motor fuels consumption can be met with corn-derived ethanol. However, 2012 drought impacted corn prices which increased ethanol production costs and constrained profitability. Ethanol plants are starting to close or operate under reduced capacity due to unprofitability. For biofuels to compete with petroleum more efficient methods of production are desperately needed by the corn ethanol industry to maximize product returns and switch product mix depending upon market prices. The concept of integrated corn/soybean biorefinery could be a strategy to increase profitability of corn ethanol industry. Enzyme-assisted Aqueous Extraction Process (EAEP) is an environment friendly alternative to chemical (n-hexane) and mechanical (screw pressing) oil extraction technologies that facilitates 97% oil recovery from soybean and produces co-products such as skim (high in protein) and insoluble fiber (high in carbohydrates). Skim and insoluble fiber can be used in dry-grind corn ethanol plants to increase rate of fermentation and ethanol yield, and improve quality of Dried Distillers Grain with Solubles *(*DDGS). In the current pathway for integrating corn/soybean biorefinery, two separate saccharification/fermentation steps are implemented in order to apply conditions for optimal ethanol production from the corn and soybean fiber source, respectively. We evaluated the addition of EAEP skim and insoluble fiber in the integrated corn/soy fermentation process and developed process model using experimental data to predict ethanol production. This poster will summarize these results.

Trimannose oligosaccharides promote pro-inflammatory response and lesion resolution during *Leishmania major* infection

Tara Grinnage-Pulley[1], Rajarshi Roychoudhury[2], Robert Schaut[1], Angela Schneider[1], Ian Lamb[1], Alex Osanya[3], Pedro Martinez[1], Nicola Pohl[2], Christine A. Peterson[1]

[1]Epidemiology, University of Iowa

[2]Chemistry, University of Iowa

[3]Veterinary Pathology, University of Iowa

Abstract

Lipophosphoglycan (LPG) of the protozoan parasite *Leishmania* is a key virulence factor for intracellular infection of immune cells. LPG is capped by various simple oligosaccharides however exploration of the role of these sugars in *Leishmania* infection has been limited. Synthesis of the trimannose cap sugar and mounting on latex beads provided a unique model to evaluate impact of these caps on the immune response. In vitro incubation of trimannose coated beads with J774 and bone marrow macrophages decreased IL-12p40 secretion suggesting that these cap sugars promote *L. major* survival. However, when *L. major* and trimannose coated beads were co-inoculated into footpads of C57BL/6 mice, production of IL-12p40 and other Th1 cytokines was up-regulated 48h post-infection. Weekly treatment with trimannose coated beads decreased lesion size in mice initially co-inoculated with trimannose beads and *L. major* when lesion size was compared to those of non-treated, infected mice. This Th1 pro-inflammatory response was mediated by uptake through mannose and TLR2 receptors as blockade of these receptors via antibodies or TLR2 deficient mice decreased effects on cytokine secretion. Trimannose oligosaccharide treatment promotes a Th1 response to alter the course of *L. major* infection.

The Myc mystery: sequence specificity vs genome-wide occupancy

Jiannan Guo[1], Tiandao Li[1], Joshua Schipper[2], Kyle A. Nilson[1], Raluca Gordân[2], David H. Price[1]

[1]Biochemistry, University of Iowa

[2]Duke University

Abstract

The Myc-Max heterodimer is a DNA binding protein that regulates expression of a large number of genes. Genome occupancy of Myc-Max is thought to be driven by E-boxes (CACGTG or variants) to which the heterodimer binds in vitro. By analyzing ChIP-Seq datasets, we demonstrated that the positions occupied by Myc-Max across the human genome correlate with the RNA polymerase II (Pol II) transcription machinery better than with E-boxes. Metagene analyses showed that in promoter regions, Myc was uniformly positioned about 100 bp upstream of essentially all promoter proximal paused polymerases with Max about 15 bp upstream of Myc. We re-evaluated the DNA binding properties of full length Myc-Max proteins using electrophoretic mobility shift assays (EMSA) and universal protein-binding microarrays (PBM). EMSA results demonstrated Myc-Max heterodimers have high affinity for both E-box containing and non-specific DNA. Quantification of the relative affinities of Myc-Max for all possible 8-mers using PBM assays showed that sequences surrounding core 6-mers significantly affect binding. Comparing to the in vitro sequence preferences, Myc-Max genomic occupancy measured by ChIP-Seq was largely, although not completely, independent of sequence specificity. Our results suggest that the transcription machinery and associated promoter accessibility play an important role in genomic occupancy of Myc.

Regulation of RNA Polymerase II Termination by Phosphorylation of Gdown1

Jiannan Guo[1], Michael E. Turek[1], David H. Price[1]

[1]Biochemistry, University of Iowa

Abstract

Gdown1 is a substoichiometric subunit of RNA polymerase II (Pol II) that has been recently demonstrated to be involved in stabilizing promoter proximal paused Pol II. It was shown to inhibit termination of Pol II by TTF2 as well as block elongation stimulation by TFIIF. Here, using in vitro transcription assays, we identified two functional domains in Gdown1. While both are required to maintain a tight association with Pol II, the N- and C-terminal domains are responsible for blocking TTF2 and TFIIF, respectively. A highly conserved LPDKG motif found in the N-terminal domain of Gdown1 is also highly conserved in TTF2. Deletion of this motif eliminated the TTF2 inhibitory activity of Gdown1. We identified a phosphorylated form of Gdown1 with altered mobility in SDS-PAGE that appears during mitosis. A kinase in HeLa nuclear extract that caused the shift was partially purified. In vitro, Gdown1 phosphorylated by this kinase demonstrated reduced activity in blocking both TTF2 and TFIIF due to its reduced affinity for Pol II. Mass spectrometry identified S270 as the site of this phosphorylation. An S270A mutation was not phosphorylated by the partially purified kinase and an S270E mutation partially mimicked the properties of phospho-Gdown1. Gdown1 S270 phosphorylation occurs predominately during mitosis, and we suggest that this would enable TTF2 to terminate all Pol II even if it is associated with Gdown1.

Pedal Portal: A naturalistic study of child bicyclist behaviors and risk exposure

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Abstract

Purpose: Half a million U.S. emergency department visits each year are a result of bicycling injuries, but little is known about contributors to those injuries, especially among children. The purpose of this study was to examine characteristics and risk associated with child bicycling. **Methods:** Ten children were enrolled between August and October of 2013. Each child was equipped with a helmet-mounted GPS-enabled camera. Eligible participants lived in Johnson County, Iowa, and regularly rode their bicycles four or more times per week. Participants completed demographic questionnaires, recorded all their bicycle trips for seven consecutive days, and completed trip diaries. Trip data were aggregated to obtain error, near miss, and crash rates and distributions of riding behavior, ride type, day, time, length, duration, and purpose. **Results:** Average child rider age was 12 (SD 0.8). Average number of trips per week was 11.7 (SD 6.7). The majority of trips were commutes to school (n = 63, 53.9%), riding alone (n = 68, 58.1%), on sidewalks or side paths (56.9%), with riding behavior as a pedestrian (56%). Average trip distance was 1.2 miles (SD 1.3). Riding errors (0 to 0.06 per mile), near misses (0.05 per mile), and crashes (0.05 per mile) were low. **Conclusions:** This is the first study to estimate child rates of risky behaviors and events through the use of naturalistic data. Results provide objective measurements of child riding behaviors and risk, showing that children most often ride alone, on sidewalks, and have low rates of risky events relative to exposure.

A Genome-Wide Targeted Capture Approach for DNA Methylation Study

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Abstract

Stress is a significant risk factor for mood and anxiety disorders. An important avenue through which stress could contribute to these disorders is by altering DNA methylation patterns. Presently, genome-wide methylation studies depend on techniques such as the use of DNA methylation-sensitive enzymes and immuno-affinity enrichment of DNA methylated regions. In this study, we used a novel genome-wide DNA methylation assay called Methyl-Seq to increase sequencing depth for DNA methylation detection at base pair resolution while minimizing sequencing costs. This assay targets ~100 MB focusing on promoters, transcription regulatory elements and known differentially methylated regions. To demonstrate the validity of this approach, we investigated tissue-specific DNA methylation patterns across liver (N=3) and different brain tissues (hippocampus, N=3; cortex, N=3). We generated 50 million reads using the Illumina HiSeq. After filtering, 90% of bases were on targeted regions. Average depth of coverage was ~45X. Methylation levels across technical replicates showed low variation, at ~10%. Tissue-specific DNA methylated cytosines (DMCs) were more prominent outside of CpG islands with the highest frequency observed in CpG open sea. DMCs were more common in intergenic and intronic regions than in exons. Importantly, differentially methylated regions were validated independently by bisulfite pyrosequencing in 17 of 21 regions tested demonstrating the reliability of Methyl-Seq. For example, Apcdd showed 38% difference in methylation between hippocampus and cortex using Methyl-Seq, and 26-39% difference in two cohorts by pyrosequencing. This method can be used to identify candidate regions for differential DNA methylation in a stress-induced mouse model of depression.

Lipid-overload impairs lysosomal enzyme activity and autophagosome turnover by inducing Protein kinase C (PKC)-NADPH oxidase 2 (NOX2) Pathway

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Abstract

Obesity regulates autophagy in a tissue-specific manner that influences tissue homeostasis. The regulation of cardiomyocyte autophagy in obesity is incompletely understood. High-fat feeding increased autophagosome number in the adult murine heart and treatment of mice with chloroquine (CQ) did not further increase autophagosome numbers suggesting impaired turnover. To elucidate the underlying mechanisms H9C2 cardiomyocytes (CM) were incubated with vehicle (veh) or 500 µM palmitate (PAL) for 4h. PAL treatment significantly induced autophagosome abundance as revealed by an increase in LC3-II levels (~2.5 fold) and autophagosome number (~4-fold) relative to vehicle treatment. Inhibition of autophagosome turnover with CQ led to the accumulation of LC3-II and autophagosomes to a greater extent in veh-treated CMs than in PAL-treated CMs relative to their respective saline-treated controls. PAL significantly induced superoxide generation (~3.8 fold) and impaired lysosomal acidification and lysosomal Cathepsin L (CatL) activity. Treatment with the superoxide scavenger tiron significantly reduced LC3-II levels (~35%) in PAL-treated CMs and restored lysosomal acidification and Cat L activity. Moreover, inhibition of NOX2 activity by siRNA-mediated depletion of its regulatory subunit p47phox or by apocynin significantly reduced LC3-II levels (~31%), normalized autophagosome accumulation and CatL activity and suppressed superoxide generation to basal levels. PAL induced NOX2 activity by facilitating the translocation of p47phox to the plasma membrane which was partially blunted by the inhibition of PKC-α/βII with Gö6976. Inhibition of PKC-α/βII prevented the accumulation of LC3-II (~37%), restored Cat L activity and suppressed superoxide production to basal levels in PAL-treated CMs. Consistent with *in vitro* data, membrane translocation of p47phox was significantly increased in HFD-fed murine hearts relative NCD-fed controls (~47%) suggesting NOX2 activation upon high-fat feeding. Thus, activation of a PKC-NOX2 pathway represents a novel mechanism that impairs lysosomal acidification and enzyme activity leading to inhibition of autophagosome turnover in lipid-overloaded CMs.

Influence of weather and swath density on drying rate potential of corn stover

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Abstract

In-field drying rate of corn stover is influenced by environmental factors, crop architecture and harvest methods. Environmental factors are difficult to control in field conditions and might require several years of experimentation. Simulation of biomass field drying using environmental chamber can provide better understanding of processes and factors governing the drying process. An environmental chamber was designed to simulate the conditions present in the field. Different weather conditions of radiation intensity, vapor pressure deficit, wind speed and swath thickness were tested and its effect on drying rate was evaluated. Air at controlled temperature and humidity was supplied by an air conditioning unit. Wind speed and solar radiation was controlled by using variable speed fan and infrared lamps, respectively. Trays were filled with different quantities of corn stover to simulate different swath densities obtained during the harvesting process. Weight of the trays were recorded after every two minutes to estimate the drying rate at particular environmental conditions. The results obtained can be used for various simulation models for biomass handling, storage and transportation.

Metformin, inflammasome activation and the IL-1/IL1R1 axis in obesity associated breast cancer progression

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Abstract

Obesity is a known risk factor for breast cancer and is associated with poor clinical outcome. Many hypotheses have been proposed to explain the link between obesity and breast cancer, however the mechanism remains unclear. We focus on the role of obesity-associated chronic inflammation, as obesity and inflammation are known risk factors for many of the same chronic diseases including type-2 diabetes and cancer. We are particularly interested in the role of the IL-1/IL1R1 axis and its upstream inflammasome activation as it can regulate the expression of many other pro-inflammatory cancer-promoting cytokines/chemokines. Using a syngeneic orthotopic transplant model for breast cancer, we show that obese mice (mice fed with high-fat diet) have increased tumor growth and metastasis compared to normal mice. Furthermore, tumors from obese mice have increased levels of IL-1b, IL1R1, and Casp1 and increased Casp1 activation. Additionally, blocking IL-1 signaling and genetic depletion of Casp1 or NLRC4 reduce tumor growth in obese mice. Previous studies have shown that metformin, the first-line drug used to treat type-2 diabetes and known to reduce the incidence of breast cancer, can reverse or prevent the inflammation associated with obesity. We therefore treated mice with metformin to determine the effect on obesity-associated tumor growth. Treatment of obese mice with metformin reduces tumor growth, showing a phenotypic resemblance to Casp1 deficient or anti-IL1R1 antibody treated obese mice. This data suggests that metformin may inhibit obesity-associated tumor growth through the same mechanism; either by directly targeting the IL-1/IL1R1 axis or reducing the metabolic stress response that stimulates inflammasome activation. In conclusion, our data suggests that inflammasome mediated IL-1 signaling promotes breast cancer progression in obese mice. Targeting inflammasome activation, neutralizing IL-1 signaling, or treatment with metformin represents a rational therapy to treat obese patients with breast cancer.

Integrating Dynamically-Downscaled Climate Simulations into an Iowa Watershed Model for Forecasting Climate Change Impacts on Water

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Abstract

Energy and water maintain a complex relationship because energy production consumes water, while water production and distribution consume energy. One example of this energy-water nexus is the impact of energy consumption on water resources through climate change. The emission of greenhouse gases from energy consumption impact the climate, which in turn impacts hydrology. To investigate the potential impacts of climate change on water resources in Iowa, a watershed model based on the Hydrological Simulation Program in Fortran (HSPF) was developed for the North Skunk River. A dynamically-downscaled climate hindcast using the Standard Weather Research and Forecasting Model for North America was used to force the climate from 1985-2005. Using the climate hindcast, the hydrology model was able to reproduce the observed flow-duration curve and annual hydrograph for the watershed. The combined climate/hydrology approach can be used to forecast future impacts on water resources under different climate scenarios.

Targeting Endogenous FGF21 Activity to Enhance Insulin Sensitivity

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Abstract

The number of individuals diagnosed with diabetes and insulin resistance world-wide has reached epidemic proportions. Therefore, the development of new insulin sensitizing drugs is imperative. In this regard, fibroblast growth factor 21 (FGF21) is a recently identified hormone considered to be one of the most promising future drug candidates for the treatment of insulin resistance. The pharmacological administration of recombinant FGF21 has potent insulin sensitizing effects in obese rodents and humans (Kharitonenkov 2005; Gaich 2013). Paradoxical to this insulin sensitizing effect, circulating levels of endogenous FGF21 are elevated in obese rodents and humans suggesting that a state of "FGF21 resistance" may play a role in the etiology of obesity induced insulin resistance. FGF21 signals to tissues through a complex formed by the FGF-receptor-1 and the essential co-receptor β-klotho. Although FGF-receptor-1 expression is ubiquitous, β-klotho is expressed in tissues with high metabolic demand. Although not fully understood, β-klotho expression in adipose is essential for FGF21's insulin sensitizing actions (Ding et al. 2012). Our preliminary rodent studies revealed a significant decrease in adipose tissue β-klotho protein expression in parallel to elevated plasma FGF21 levels during the development of diet induced obesity suggesting that modulation of β-klotho protein expression in this tissue may play a key role in controlling FGF21 activity. Our goal is to uncover the mechanisms by which β-klotho regulates FGF21 activity under physiological and patho-physiological states. Understanding these mechanisms will allow us to therapeutically target β-klotho expression as a strategy for restoring endogenous FGF21 activity thus enhancing insulin sensitivity.

New Approaches in Mesoscale Modeling

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Abstract

Coarse-grained models that are rigorously derived from all-atom molecular simulation trajectories can be successfully implemented in molecular dynamics simulation to reproduce the structure and thermodynamics of the all-atom reference system. Dynamic properties from these coarse-grained molecular simulations are often unreliable because the reduction in degrees of freedom eliminates much of the friction between coarse-grained beads. This results in faster dynamics for the coarse-grained simulation. This is an advantage when it comes to efficient sampling of phase space but problematic if accurate computation of one or more time-dependent properties is a desired outcome from the coarse-grained simulation. In this work, a new approach is developed for deriving coarse-grained intermolecular forces. This approach retains the frictional contribution that is often discarded by conventional coarse-graining methods. This method is based on the well-known Langevin equation formalism. Compared to previous implementations of the Langevin equation for coarse-grained dynamics, in this method, the friction coefficients are computed directly during the derivation of the CG force field, using routine post-processing calculations. The procedure is tested for water and an aqueous glucose solution, and the results from the new implementation for coarse-grained molecular dynamics simulation show remarkable agreement with the dynamics obtained from reference all-atom simulations. The agreement between the structural properties observed in the coarse-grained and all-atom simulations is also preserved. We discuss how this approach may be applied broadly to any existing coarse-graining method where the coarse-grained models are rigorously derived from all-atom reference systems.

Isolation and Analysis of Ngn3/CD133+ Endocrine Precursor Cells From Human Exocrine Tissue

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Abstract

Type I Diabetes Mellitus (T1DM) is a metabolic disease caused by the autoimmune destruction of insulin-producing beta cells in human pancreatic islets. Human islet transplantation is now seen as a viable treatment against T1DM, however the procedure is limited due to the lack of availability of pancreata from human donors. At present the vast majority of donor pancreas tissue, mainly comprised of exocrine tissue (non-islet cell tissue), is discarded following the isolation of islet cells from the organ. During pancreatic development, cells that commit to an islet cell fate, including the insulin producing beta-cells begin to express a transcription factor Neurogenin 3 (Ngn3). Furthermore these Ngn3+ cells in the human pancreas co-express CD133, a transmembrane glycoprotein. We set about to isolate CD133+ cells, isolated from exocrine tissue discarded during human pancreatic islet isolations, which are also known to express Ngn3. These individual cells were shown to aggregate into sphere like structures, known as pancospheres. Histological analysis of the pancospheres indicated the presence of Pdx1, a transcription factor necessary for islet development. Furthermore *in vivo* analysis of these pancospheres in nude mice indicated an alteration in blood glucose levels. Together these data indicate that endocrine precursor cells can be isolated from "waste" exocrine tissue following human pancreatic islet isolation and that such cells, when cultured, can develop into pancospheres that can express proteins necessary for pancreatic development and beta-cell maturation. Further in-depth genetic, proteomic and functional analysis of these pancopheres will have to be performed to determine their exact significance to the field of diabetic research.

Engineered Nanomaterials in Aqueous Environments: Interactions, Transformations and Implications

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Abstract

Nanoscience and nanotechnology offer potential routes towards addressing critical issues such as clean and sustainable energy, environmental protection and human health. Specifically, metal based nanomaterials are found in a wide range of applications and therefore hold a greater potential of possible release into the environment or for the human to be exposed. Understanding the aqueous phase behavior of metal and metal oxide nanomaterials is a key factor in the safe design of these materials because their interactions with living systems are always mediated through the aqueous phase. Broadly the transformations in the aqueous phase can be classified as dissolution, aggregation and adsorption which are dependent and linked processes to one another. The complexity of these processes at the liquid-solid interface has therefore been one of the grand challenges that have persisted since the beginning of nanotechnology. Therefore currently the environmental health and safety studies related to nanomaterials are more focused on understanding the surface chemistry that governs the overall processes in the liquid-solid interfacial region at the molecular level. Specifically, the interactions of metal and metal oxide nanoparticles with environmental and biological ligands in the solutions have demonstrated dramatic alterations in their aqueous phase behavior in terms of dissolution and aggregation. Furthermore, solution conditions such as ionic strength and pH can act as controlling parameters for surface ligand adsorption while adsorbed ligands themselves undergo surface induced structural and conformational changes. Because, nanomaterials in both the environment and in biological systems are subjected to a wide range of matrix conditions they are in fact dynamic entities. Therefore this research attempts to bridge the gap between the dynamic processing of these nanomaterials, the details of the molecular processes that occur at the liquid-solid interfacial region and potential interactions.

Measuring Mechanical Properties of the Pancreas in Vivo

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Abstract

Pancreatic cancer is the fourth most common cause of cancer-related deaths in the United States with the one- and five-year survival rates of 25% and 6% respectively. We have been investigating the use of shear wave vibrometry to quantify mechanical properties of 4 excised pig pancreases. In addition, we performed *in vivo* transabdominal measurements of shear wave velocity and attenuation of the pancreas in a pig. Ultrasound was focused in the pancreas to excite impulsive shear waves and track the motion of the tissue. Fourier space analysis was used to calculate the shear wave velocity and attenuation in the pancreas. We studied shear wave propagation at several different locations in 3 excised porcine pancreases and repeated each measurement 5 times. In addition, we submerged an excised pig pancreas in a formalin bath and measured the shear wave velocity and attenuation every 20 minutes for a total of 100 minutes. Measurements in the *in vivo* pig pancreas were performed both trans-abdominally and with an open abdomen allowing a direct acoustic access to the organ. In the formalin and the *in vivo* studies, shear wave velocity and attenuation were measured at 100 Hz. The formalin studies showed that the velocity increased from 0.5 m/s at t = 0 minutes to 1.1 m/s at t = 100 minutes, while the attenuation decreased from 400 Np/m to 200 Np/m. The formalin studies suggest that shear wave vibrometry can track changes in pancreatic shear wave velocity and attenuation. *In vivo* transabdominal values of shear wave velocity and attenuation at 100 Hz were c = 1.07 m/s and α = 173 Np/m. The *in vivo* open-abdomen values were c = 1.14 m/s and α = 170 Np/m. These results demonstrate the feasibility of using shear wave vibrometry to assess mechanical properties of the pancreas.

Medial frontal D1 dopamine signaling is required for low-frequency oscillations and ramping neural activity during interval timing

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Abstract

Organizing behavior in time is a fundamental process that is highly conserved across species. Patients with human diseases involving dopamine signaling have impairments in the temporal organization of behavior. Previous work has shown that signaling via the D1 dopamine receptor in medial frontal cortex (MFC) is required for temporal control of action. Here, we tested the hypothesis that D1 signaling is necessary for MFC neural activity encoding time. First, we found that humans and rodents had similar bursts of stimulus-triggered low-frequency oscillations in MFC. Focal MFC D1 blockade eliminated both low-frequency oscillations and coupling between MFC field potentials and single neurons. Finally, MFC D1 blockade eliminated ramping neuronal activity that was correlated with behavior. These data provide novel evidence demonstrating that D1signaling controls temporal processing within MFC and illuminates neural circuitry controlling the temporal organization of mammalian behavior.

Rational Synthesis of Zintl Phases: A still challenging Task

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Abstract

The development of conceptual models for rationalizing the diversity or guiding the crystal structures of intermetallic compounds has remained very challenging, despite the very fast expansion of their rich structural chemistry, powered by an intense exploratory synthesis.

Wind farm wake detection from surface measurements during the 2013 Crop Wind-energy Experiments (CWEX-13)

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Abstract

In situ measurements within utility-scale wind farms facilitate documentation of wind farm under-performance and the data provide calibration benchmarks for numerical and wind tunnel simulations of flow fields (i.e. wakes) from wind turbines and wind farms. In the 2013 Crop Wind-energy Experiment (CWEX-13), seven surface flux stations and three wind-profiling LiDARs (Light detection and ranging) measured wind speed, turbulence, and wind direction above several soybean fields within the northwest third of a 300 MW Iowa wind farm from early July to middle September. Surface fluxes are analyzed to detect changes in wind speed, wind direction, and turbulent mixing at several downwind stations when compared to a reference station upwind of the first turbine line for a prevailing south wind direction. Southerly winds document turbine wakes for a few lines of turbines, whereas winds from the west to northwest and the southeast illustrate an aggregate effect of multiple lines of turbines perturbing surface flow fields. Wind speed is reduced by as much as 50% at several stations downwind of multiple turbine lines for daytime, windy conditions. In nighttime low wind speed conditions, turbine wakes increase the surface wind speed by a factor of two, and turbulent mixing by as much as factor of five of the ambient properties at the reference station. Directional deflection at the surface is as large as 30-40 degrees downwind of a few lines of turbines during the nighttime but the effects are more variable during daytime. The surface analyses highlight the importance of characterizing turbine wake measurements according to several atmospheric factors (e.g. thermal stratification, wind direction, wind speed) and for multiple regimes of wind farm interaction (e.g. first turbine line, second line of turbines, multiple turbine lines, and clusters of many turbine lines).

Reproducibility of Total Retinal Thickness in 5 SD-OCT Scanners using Iowa Reference Algorithm

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Abstract

Purpose: A comparison of total retinal thickness (TRT) measurements is presented using the Iowa Reference Algorithm from 5 commercially available Spectral-Domain Optical Coherence tomography (SD-OCT) scanners. **Methods:** Fovea-centered SD-OCT volumes from 11 subjects were obtained at the Vienna Reading Center, Austria: 4 normal, 1 atrophic AMD, 1 macular hole, 2 Stargardt's, 3 atrophic CNV. Serial-imaging OCT scans (all 6×6×2 mm^3) were obtained using: CirrusTM HD-OCT (Carl Zeiss Meditec, 512×128×1024 voxels), RTVue (Optovue, 513×101×640), RS 3000 (Nidek, 512×128×512), Heidelberg Spectralis® (Heidelberg Engineering, 512×49×496), Topcon (Topcon, 512×128×885). The Iowa Reference Algorithm, which routinely segments 10 retinal layers, measured TRT as the average of all the A-scan voxels between inner limiting membrane and Bruch's membrane surfaces. The model of TRT measurement comparisons across the five SD-OCT devices is $X_{mi}=\alpha_m+ß_m\mu_i+\varepsilon_{mi}$. X_{mi} is a measurement from a device expressing the true value μ_i with intercept and slope $ß_m$, ε_{mi} with having mean=0 and variance=1 . This model is more general than limit of agreement analysis, as $ß_m$ are not required to be the same and equal to 1. Mendel test was employed to investigate whether the five $ß_m$ values are the same. Bland Altman plots are provided and 5 SD-OCT pairwise predictive equations expressed via method comparison, using "additivityTests" and "MethComp" from the R package. **Results:** Mendel test on the proposed model reveals that the five $ß_m$ expressing that the differences among the TRT measurements are constant (p=0.992). Ten pridictive equations were estimated, which give the inter-scanner TRT measurement conversions in a pair-wise manner. **Conclusions:** The achieved p-value of 0.992 with the proposed model for 5 SD-OCTs establishes the cross-scanner reproducibility of the Iowa Reference algorithm. TRT measurements are highly reproducible, thus facilitating multi-center studies with heterogeneous device utilization.

Midwest Postdoctoral Forum (MDWPDF), an excellent model for a regional collaboration among postdoctoral communities

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Abstract

Scarcity of networking among postdoctoral communities in the Midwest encouraged us to form a regional forum to: 1) Bring their various perspectives into such platform for efficient and innovative regional cooperation; and, 2) Promote communication amongst them by facilitating collaboration in social and professional areas, especially where the resources of individual institutions are limited. Midwest Postdoctoral Forum (**MWPDF**) started in June 2012 in Ames, IA, at a brainstorming meeting among official representatives of regional postdoctoral communities (**PDAs**), including but not limited to Ames National Lab, Argonne National Lab, Iowa State University, Mayo Clinic, University of Iowa, University of Kansas Medical Centers, University of Nebraska-Lincoln and Wright State University. MWPDF has an outline approved by its member institutes. No dues exist for membership, and it is financially formed based on members' shared resources. Its board consists of individual representatives officially appointed from member PDAs whose responsibility is to provide leadership and continuity to the MWPDF. The board meets regularly, either via e-conference or at regional events. This forum has been used as a platform to share: 1) experiences: i.e. adapting successfully implemented policies used by individual members at other member institutes; 2) information: i.e. circulating announcements regarding with local/regional events; and, 3) Resources: opening local events to the PDAs from member institutes; or, sharing the costs between neighbor institutes by hosting concurrent career development workshops. This forum could be a great example model for other regions in the USA ensuring more networking and career development opportunities for the postdoc communities.

Evaluation of algal biofuel production potential using Geographic Information Systems: A review

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Abstact

Renewable energy is envisioned to satisfy future energy needs along with providing energy security and economic development. Locating bioenergy facilities is highly dependent on availability of spatially dispersed biomass feedstock. Geographic Information Systems (GIS) tools have been used for strategic decision making to locate bioenergy facilities and also to evaluate the biomass supply-demand scenarios in order to minimize overall cost of the system. Algae are the third generation bioenergy feedstocks and have shown potential for meeting future energy demands. This study reviews literature on the application of GIS techniques to estimate algae biofuel potential and locating algae production facilities. To highlight diversity of methods results, a comparative case study for the U.S was presented. A systematic methodology consisting of identification, screening, eligibility and inclusion was used to determine the published works reviewed for this study. The literature reviewed was classified according to purpose/objective, GIS modeling approach, constraints, novelty, shared information, application and data sources. It was found that estimates vary among studies depending on the resources considered and growth models used for the analysis. The GIS analysis ranged from simple linear overlays to complex cost-distance analysis. Number of resources such as water type, land, and CO_2 source locations considered in the study significantly affects productivity potential. None of the studies considered infrastructure requirements such as electricity, roads, rail etc. which can provide realistic estimates. Studies provide wide range of estimates for algae biofuel potential and the variation is mainly due to approaches, methodologies, assumptions and data inputs used for analysis. It can be concluded that these studies are helpful in understanding the scale of algal biofuel potential and provides opportunity for future research.

Role of human nectin-4 and F-actin in cell-to-cell spread of measles virus in airway epithelial cells

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Abstract

Measles virus (MV) is a highly contagious acute respiratory disease that continues to be a worldwide health burden. Unlike MV infection of immortalized cells, MV infection of well-differentiated primary cultures of airway epithelial cells from human donors (HAE) does not result in syncytia formation. In HAE MV infection results in the formation of infectious centers that recapitulate viral spread *in vivo*. We previously demonstrated that MV has an overwhelming preference for entry at the basolateral surface in HAE cells and use nectin-4 as a surface receptor. Cytoskeleton proteins have been shown to play a role in MV production but its role in MV spread is not known yet. Here we investigate the requirement of nectin-4 and the cytoskeleton in the process of MV cell-to-cell spread in primary epithelia. We constructed multiple human nectin-4 mutants designed to mis-localize the receptor to alternate cell-surface regions. Furthermore to investigate the role of cytoskeleton proteins during MV infection, airway cells were treated either with cytoskeleton disrupting or stabilizing drugs and MV infection was monitored. In addition the location of afadin, a bridge protein connecting nectin-4 to the actin cytoskeleton together with F-actin during MV infection was monitored. Our data suggest that nectin-4 need not be localized to adherens junctions to mediate infection and that nectin-4 is required for the initial infection of airway epithelial cells, but not for lateral spread. MV infection studies in the presence of different cytoskeletal drugs indicated that disruption of the F-actin attenuates MV infection whereas stabilizing the F-actin helps in MV infection and spread. Whereas disruption of microtubule structures after the MV infection attenuates the MV infection and spread. These results suggest that MV requires the intact cytoskeleton for successful infection and spread.

Runx2 exerts differential response in growth factors- or hormone-induced signaling in normal or metastatic breast cancer models

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Abstract

Most cancer-related deaths occur due to metastasis. In metastatic microenvironment, the signaling via growth factors promotes cancer survival, so understanding aberrant signaling mechanisms is critical for developing novel therapeutics. The Runt-related transcription factor, Runx2, is indispensable for normal bone development and is expressed in normal mammary glands where it regulates differentiation. However, Runx2 is aberrantly expressed at higher levels in metastatic breast cancers, wherein it regulates survival and invasive properties. Such context-dependent functions of Runx2 are still not completely understood and could be due to Runx2-dependent differential signaling crosstalk. To elucidate the differential functions of Runx2, we ectopically increased Runx2 levels in normal-like MCF-10A cells, while knockdown high Runx2 in bone metastatic MDA-MB-231 cells, and mimicked the metastatic microenvironment via response to growth factor signaling. The ectopic Runx2 expression in MCF-10A cells increased insulin-like growth factor (IGF) receptor (IGF1R) or Epidermal Growth Factor (EGF) receptor (EGFR) expression, but blocked EGF- or IGF-induced pErk1/2 and pAkt, the effectors of Mitogen Activated Protein Kinase (MAPK) and Phosphatidyl Inositol 3' Kinase (PI3K) signaling pathways respectively. In contrast, Runx2 inhibited IGF1R and pAkt, but increased pErk1/2 expression levels upon IGF stimulation in bone metastatic MDA-MB-231 cells. Therefore, we pharmacologically targeted pErk1/2 in bone metastatic MDA-MB-231cells with Runx2 knockdown to determine the cell survival response. To this end, the treatment with Erk1/2 inhibitor PD184161 reduced cell proliferation and clonogenic potential in-vitro and survival in ex-vivo bone culture models. Furthermore, we identified the mechanism of Runx2-mediated Erk1/2 regulation by showing that Runx2 directly regulates beta-Arrestin, an adapter protein critical for Erk1/2 activation. Altogether, our studies indicate differential Runx2 functions in normal or metastatic breast cancer cells, and suggest that the survival of bone metastatic cancer cells could be effectively blocked by inhibition of Runx2 and Erk1/2.

Deficiency of C-Jun-N-Terminal Kinase Prevents Angiotensin II-Induced Inward Remodeling but Not Hypertrophy in Cerebral Arterioles

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Abstract

Angiotensin II (Ang II) is an important determinant of inward remodeling in cerebral arterioles. We examined the effect of c-Jun-N-terminal kinase (JNK) deficiency on structural alterations in cerebral arterioles induced by Ang II. Three month old JNK1-deficient (JNK1-/-) and wild-type (WT, C57BL/6J) mice were administered Ang II (1000 ng/kg/day) or saline for 4 weeks via osmotic minipumps. Systolic arterial pressure (SAP) was measured by a tail-cuff method. External diameter (ED) of maximally dilated cerebral arterioles was measured *in vivo* through an open cranial window in anesthetized mice. Cross-sectional area (CSA) of the vessel wall was measured histologically. Infusion of Ang II significantly increased SAP in both WT (148±7 vs 120±4 [saline infused] mmHg, $P<0.05$) and JNK1-/- (148±3 vs 118±5 mmHg, $P<0.05$) mice; reduced cerebral arteriolar ED in WT (57±4 vs 68±3 μm, $P<0.05$), but not in JNK1-/- mice (65±4 vs 66±4 μm, $P<0.05$); and increased CSA of the arteriolar wall in JNK1-/- (501±41 vs 388±49 μm^2, $P<0.05$), as well as WT (519±74 vs 393±30 μm^2, $P<0.05$). In conclusion, our findings suggest that JNK1 may play an important role in Ang II-induced inward remodeling, but not hypertrophy, in cerebral arterioles.

Plant Cell Wall Structure and Hydration Investigated by Sensitivity-Enhanced Solid-State NMR

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Abstract

Solid-state NMR spectroscopy has been applied to investigate the structure and dynamics of the three polymers that comprise the primary plant cell wall (CW): cellulose, hemicellulose and pectin. The plants were grown in ^{13}C-enriched media, which improved the sensitivity of the measurements by per-labeling the CW. Dynamic nuclear polarization was used to enhance the signal from microgram quantities of the plant protein expansin, which is responsible for cell wall expansion, in order to determine its binding targets. The CW 3D structure was probed by a water-polysaccharide ^{1}H spin diffusion experiment, showing that pectins are the best hydrated while cellulose the least. Extraction of pectin and hemicellulose changes the water accessibilities dramatically, giving insight into polysaccharide packing in the cell wall.

Identification of a lysozyme receptor and a new class of lysozyme inhibitors in Gram-positive bacteria

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Abstract

Clostridium difficile is an anaerobic, Gram-positive, spore-forming bacterium that causes a range of gastrointestinal diseases including life-threatening pseudomembranous colitis. *C. difficile* is linked to ~14,000 deaths per year in the US (CDC). These infections usually occur when antibiotics disrupt the normal intestinal microbiome. Given its clinical importance, relatively little is known about how this bacterium survives/resists the host innate immune system. Bacteria often utilize alternative σ factors to respond to external stress and control virulence gene expression. We have identified a putative *C. difficile* σ factor system that specifically responds to a key component of the innate immune system, lysozyme. Mutants of this system exhibit a substantially higher sensitivity to lysozyme than wild-type *C. difficile* and, interestingly, are attenuated for virulence in an animal model of *C. difficile*-associated disease. This system produces a unique lysozyme receptor and controls transcription of genes involved in modification of the cell's cell wall, contributing to lysozyme resistance. Apart from this, we also found production of receptor (RsiV), in a mutant of this system, results in increased lysozyme resistance. We show a portion RsiV directly binds lysozyme and inhibits lysozyme's enzymatic activity. This suggests the receptor has roles in *both sensing lysozyme stress and directly contributing to lysozyme resistance*. While a number of protein encoded lysozyme inhibitors have been identified in Gram-negative bacteria, RsiV shows no homology to these and would be *the first example of a lysozyme inhibitor in Gram-positive bacteria*. The presence of protein encoded lysozyme inhibitors in Gram-negative bacteria has been linked to the ability of pathogens to avoid the host innate immune response; RsiV could contribute to pathogenesis in a similar manner in *C. difficile.*

Molecular dynamics study of correlation between bulk and solid-liquid interface properties in pure metals

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Abstract

Properties of metals created by solidification from an initially molten state depend sensitively on properties of the solid-liquid interface. Experimental procedures that can accurately measure interface properties are difficult to perform. Therefore the ability to quantitatively predict interface properties from knowledge of bulk properties would be very useful in engineering metals with desirable properties. In this work, a set of interatomic potentials have been created to systematically vary specific bulk properties in pure molten metals. Solid-liquid interface properties are then determined from atomistic simulations. A direct correlation is discovered between certain bulk properties and interface properties.

Transdifferentiation off Bone Marrow-Derived Stem Cells into Schwann-like cells on Micropatterned Polymer Substrates for Peripheral Nerve Regeneration Strategies

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Abstract

Peripheral nerve injuries (PNI) can lead to serious neurological deficits resulting in sensory/motor dysfunctions. A goal of this project is to develop biodegradable nerve guidance conduits paired with bone marrow-derived mesenchymal stem cells (MSCs) to facilitate peripheral nerve regeneration. MSCs are multipotent somatic cells that are easily isolated and maintained in culture, and may be used for autologous grafting procedures. Under the appropriate conditions MSCs can be transdifferentiated into Schwann cell (SC)-like phenotypes. These cells resemble typical SC morphologically and molecularly.SCs are peripheral glia forming myelin sheath around axons of motor and sensory neurons. SCs also secrete trophic and growth factors promoting neural regeneration. However, SC harvesting requires an additional surgery and sacrifice of a donor nerve that may result in donor site morbidity.The focus of this work is to transdifferentiate rat MSCs into SC-like phenotypes on micropatterned polymer substrates, that may be used for fabricating nerve regeneration conduits. Our hypothesis is that alignment would promote peripheral nerve regeneration by orienting axon regrowth in a directed fashion. In this study we investigated transdifferentiation and alignment of the MSCs on biodegradable poly-lactic acid (PLA) micropatterned and nonpatterned films, and compared this polymer with polystyrene (PS) films. Identification of the transdifferentiated MSCs (tMSCs) was based upon immunolabeling with antibody markers used to identify SC, anti-S100β and anti-$p75^{NTR}$.The results revealed that cells aligned in the direction of the microgrooves when grown on micropatterned substrates. Substrate topography did not significantly affect the percentage of tMSCs suggesting that micropatterning does not cause any decrease in the level of transdifferentiation. In the future, we plan to use PLA films to engineer conduits that may be inserted at the site of nerve transection to promote peripheral nerve regeneration.