Unraveling Spatial & Temporal Relationships in Biological Systems

SAND2013-2409P

Advanced Analytical Imaging & Analysis Tools

Hyperspectral Fluorescence Imaging

Vibrational Spectroscopic Imaging

TIRF Microscopy

Super Resolution Microscopy

Multivariate Image Analysis

Image Correlation, Particle Tracking

Current Applications:

Host pathogen interactions

- Spatio-temporal signaling at immunological synapse (two receptor systems), membrane specific, simultaneous dual color
- Understanding virulence mechanisms in *F. Novicida*, spatial localization, protein interactions

Bioenergy

- Visualize fluorescent proteins, natural pigments in plants, goals of engineering to optimize decomposition, understanding energy transfer
- Analytical measurements for improved algal biofuels production at scale

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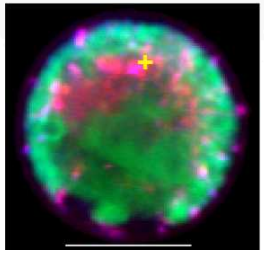
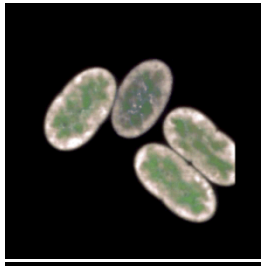
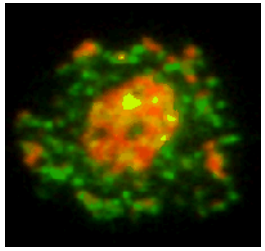
Timlin Lab Research Focus

http://bio.sandia.gov/people/timlin.html

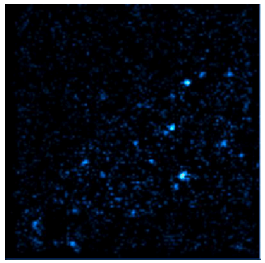


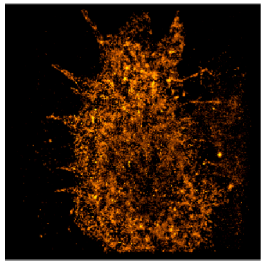


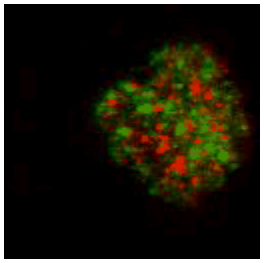


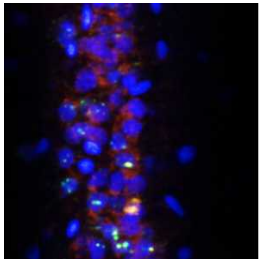
Unraveling Spatial-Temporal Relationships in Complex Multicomponent Biological Systems at Multiple Scales

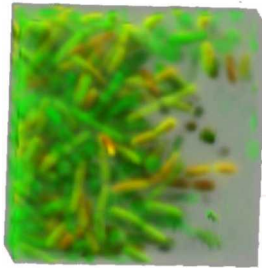
- Advanced spectroscopy
- Innovative imaging technologies
- Chemometric data analysis tools
  - Multidisciplinary
  - Cell biology, immunology, and microbiology
  - Biodefense and Bioenergy











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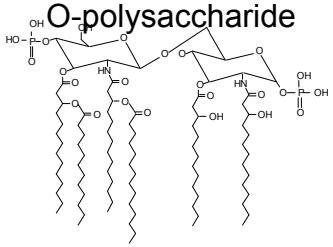
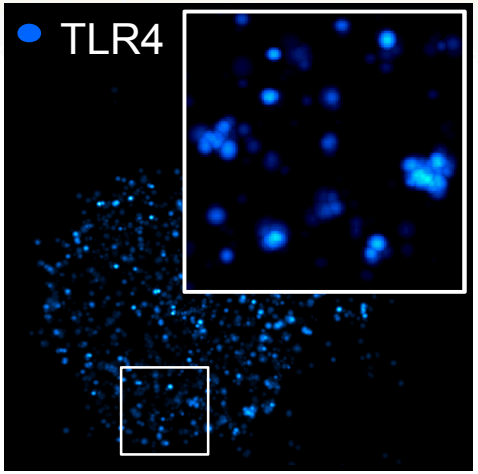
Receptor Cluster Formation in Immune Response

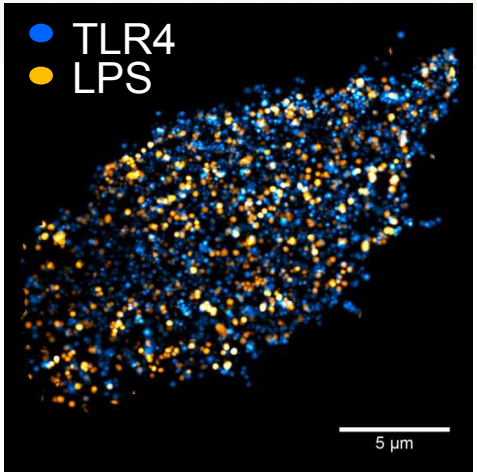
***E. coli* LPS**

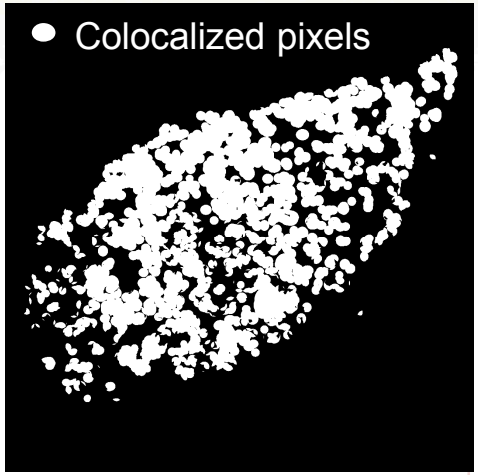
Smooth O-polysaccharide



Bind surface, stimulatory

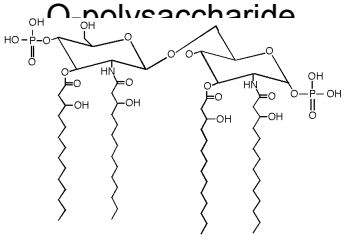




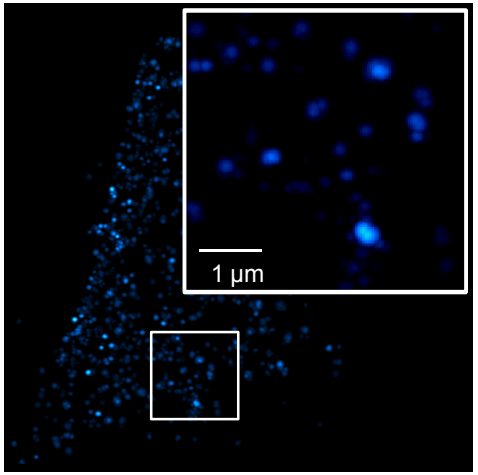


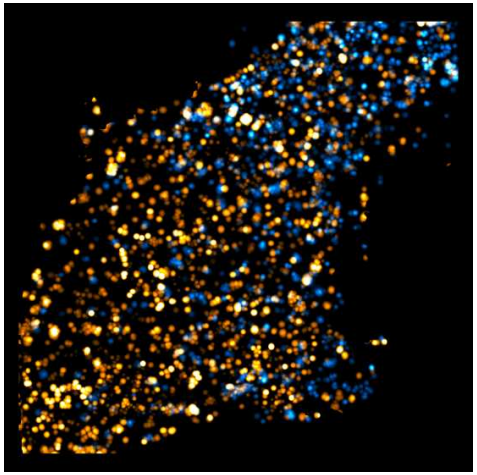
***Y. pestis* LPS (37 º)**

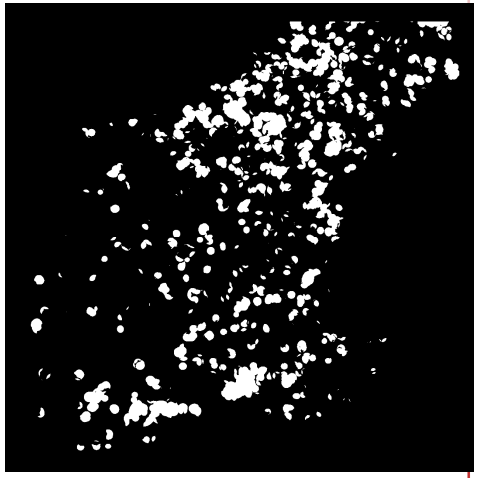
Rough O-polysaccharide



Bind surface, non-stimulatory







Aaron JS, Carson BD, Timlin JA, Characterization of Differential Toll-Like Receptor Responses below the Optical Diffraction Limit. *Small* 2012; 8(19): 3041-3049.

NIH DIRECTOR'S NEW INNOVATOR AWARD

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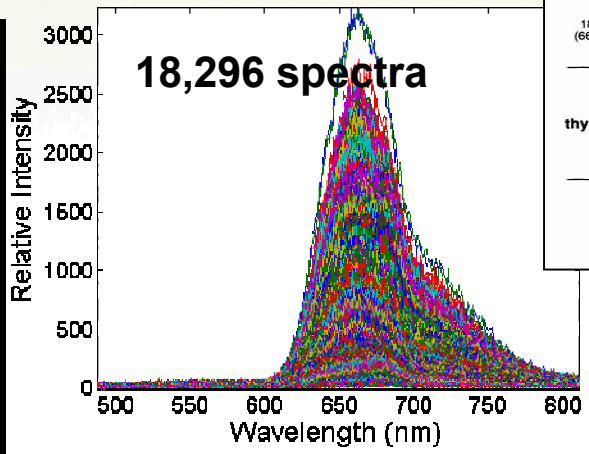
Visualization of Photosynthetic Pigments in Cyanobacteria

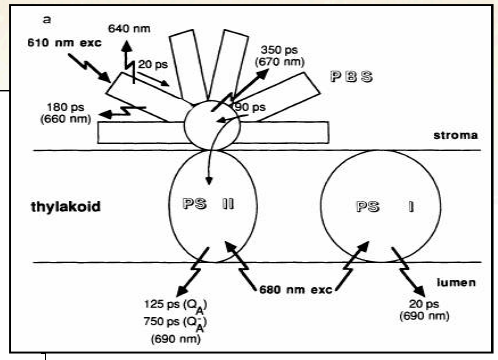
Purpose and Approach

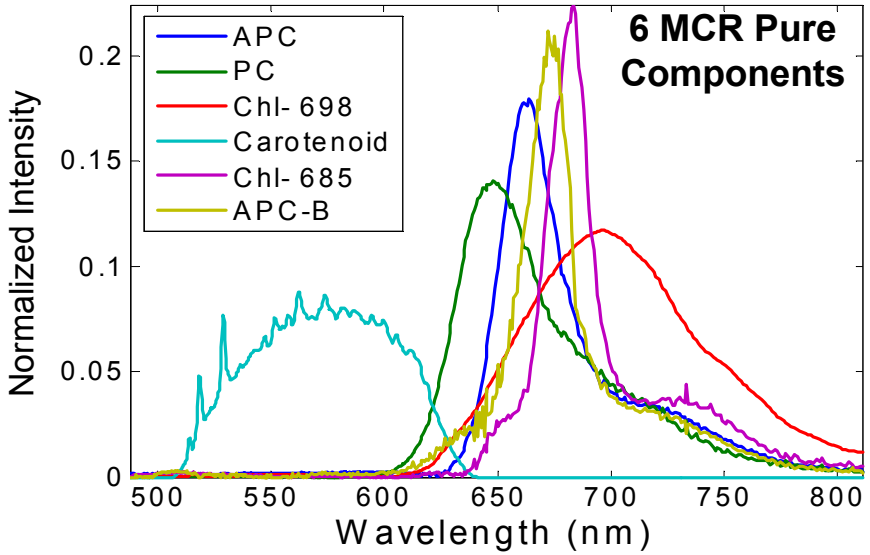
Couple confocal hyperspectral imaging with multivariate curve resolution to unambiguously identify fluorescent pigment complexes involved in energy transfer in wild-type and mutant bacteria in vivo … spectral and spatial overlap makes this impossible by any other technique

Key Accomplishments

- Developed new image analysis tools (genetic algorithms, noise models, etc.)
- Identified and mathematically separated 6 highly overlapped fluorescence species common to 7 strains/growth conditions *in vivo*
  - Tracked spatial patterns
  - Relative intensities
- Confirmed thylakoid membrane heterogeneity







WJ Vermaas, JA Timlin, HDT Jones, MB Sinclair, LT Nieman, S Hamad, DL Melgaard, and DM Haaland. 2008. "In vivo hyperspectral confocal fluorescence imaging to determine pigment localization and distribution in cyanobacterial cells." *PNAS* 105:4050-4055.

Relevant publications

- Aaron JS, Carson BD, Timlin JA "Characterization of Differential Toll-Like Receptor Responses below the Optical Diffraction Limit," Small, 2012, 8(19), 3041-3049.
- Jones HDT, Haaland DM, Sinclair MB, Melgaard DK, Collins A M, Timlin JA "Preprocessing Strategies to Improve MCR Analyses of Hyperspectral Images," Journal of Chemometrics and Intelligent Laboratory Systems, 2012, 117, 149-158.
- Collins, AM, Liberton, M, Jones, HDT, Garcia, OF, Pakrasi, HB, Timlin, JA "Photosynthetic Pigment Localization and Thylakoid Membrane Morphology are Altered in Synechocystis 6803 Phycobilisome Mutants" Plant Physiology, 2012, 158, 1600-1609.
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- Aaron JS, Greene A Kotula PG, Bachand GD, and Timlin JA. "Advanced Optical Imaging Reveals Dependence of Particle Geometry on Interactions between CdSe Quantum Dots and Immune Cells." Small, 7(3), 2011, 334-341.
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- Vermaas WJ, Timlin JA, Jones HDT, Sinclair MB, Nieman LT, Hamad S, Melgaard DK, Haaland DM, "In vivo hyperspectral confocal fluorescence imaging to determine pigment localization and distribution in cyanobacterial cells," PNAS, 105(10), 2008, 4050-4055. (PMC2268818)
- Sutherland V, Timlin JA, Nieman LT, Guzowski JF, Chawla MK, Roysam B, Worley PF, McNaughton BL, Sinclair MB, Barnes CA, "Advanced imaging of multiple mRNAs in brain tissue using a custom hyperspectral imager and multivariate curve resolution," Journal of Neuroscience Methods, 160(1), 2007, 144-148. (PMC1815393)
- Sinclair MB, Haaland DM, Timlin JA, Jones HDT, "Hyperspectral confocal microscope," Applied Optics, 45(24), 2006, 3283-3291.

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