

Cell Membrane Dynamics in Infrared Nerve Stimulation and Blocking

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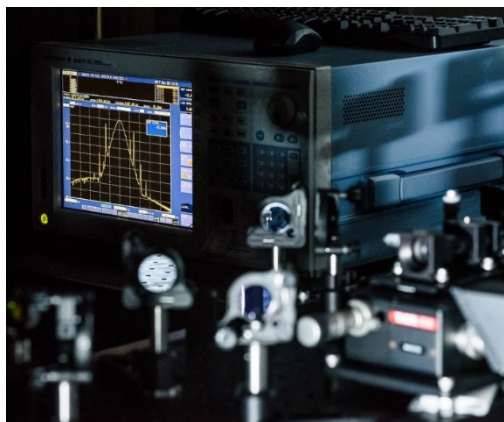
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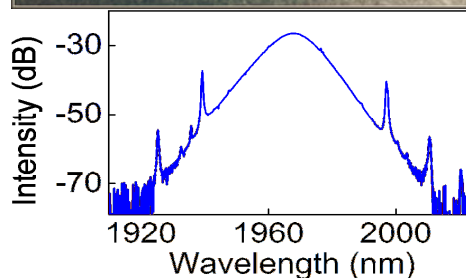
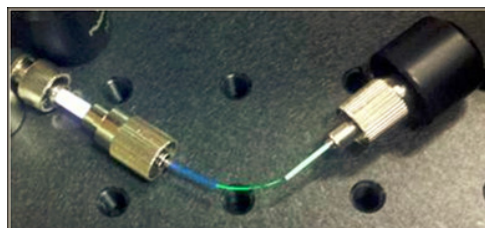
AFOSR Biophysics Review Meeting April 20, 2018

Research Group Overview

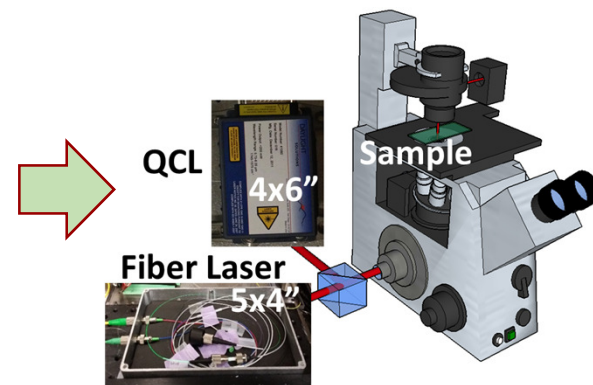
Novel Laser Design,
Ultrafast Pulse Dynamics
and Real-Time Monitoring



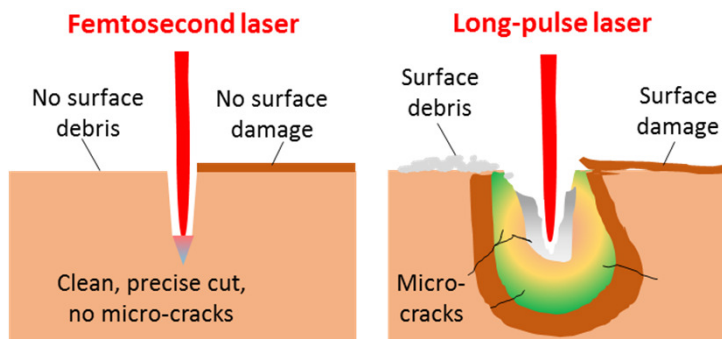
Compact Fiber Lasers



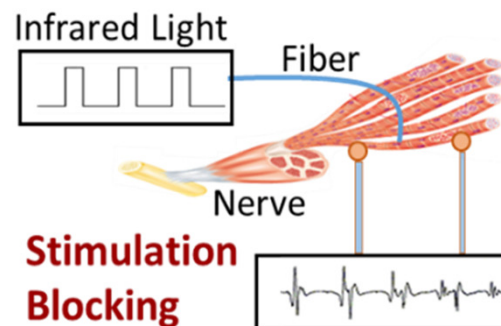
Label-Free Photothermal
Spectroscopy and Biomedical
Imaging in the mid-IR



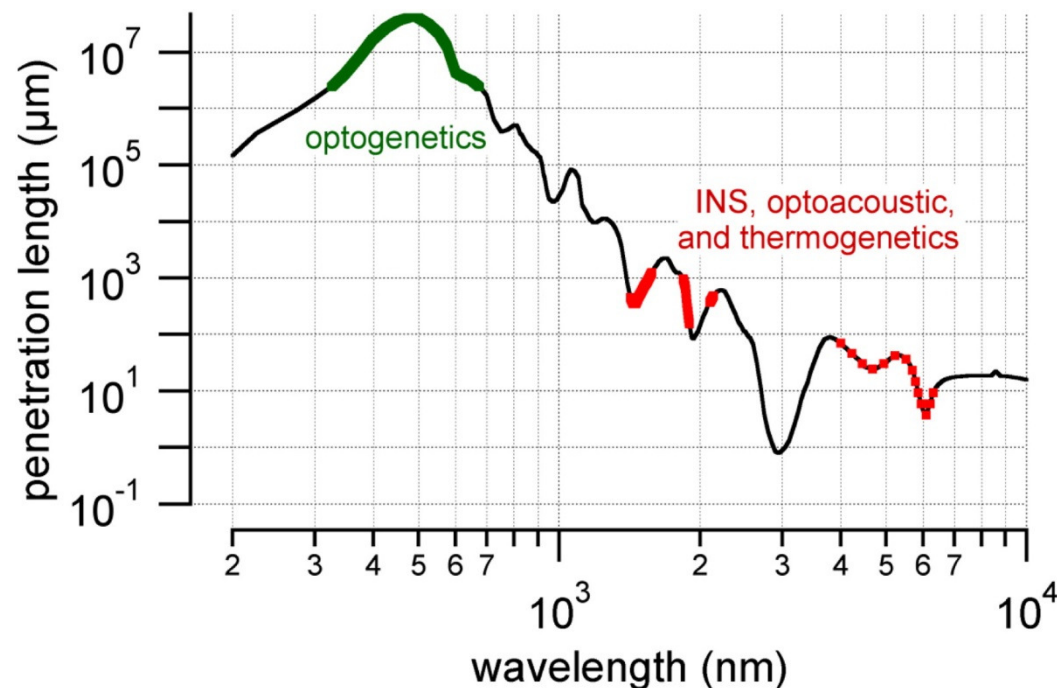
Femtosecond Micromachining



Infrared Nerve Stimulation



Why Infrared Neural Stimulation?



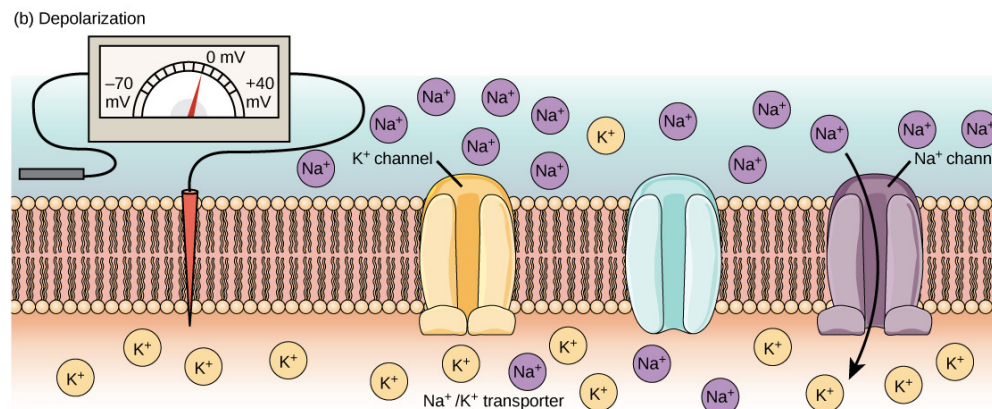
C.-P. Richter, X. Tan / Hearing Research 311 (2014) 72e88

- Relies on inherent absorption, no genetic modification needed
- High precision control with good spatial confinement
- High selectivity
- Minimal invasiveness reducing inflammation risk and necrosis
- Optical inhibition of neural signals and nerve blocks:
no stimulation artifacts or onset responses

Underlying Biophysical Mechanism

Thermal gradients lead to cell depolarization and compound action potentials

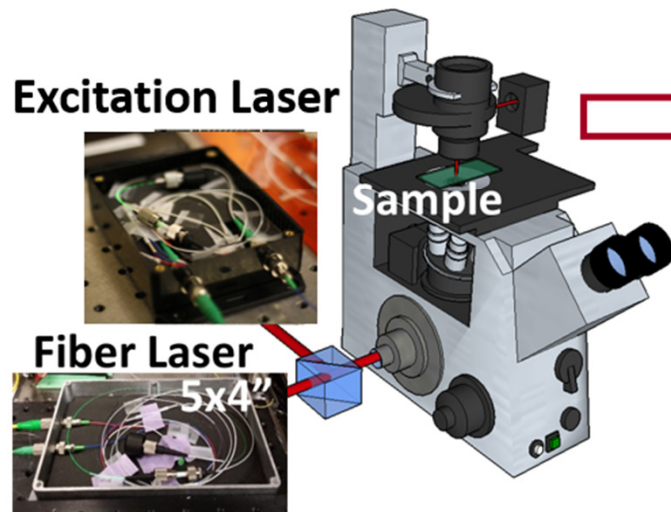
- complex interplay between multiple effects
- reversible nanopores
- transient increase/changes in membrane capacitance
- activation of thermally-sensitive channel proteins (TRPV)
- selective calcium influx: intracellular calcium released



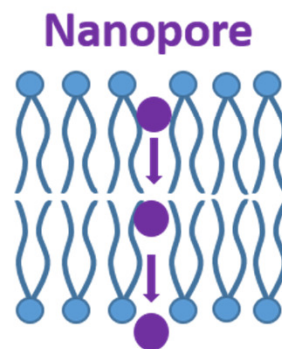
<http://cnx.org/content/m47519/1.1/>

Research Goals

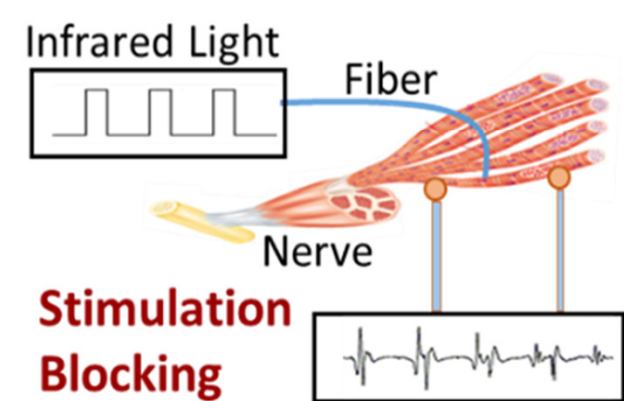
Photothermal Spectroscopy: Linear and Nonlinear



Cell Membrane Dynamics

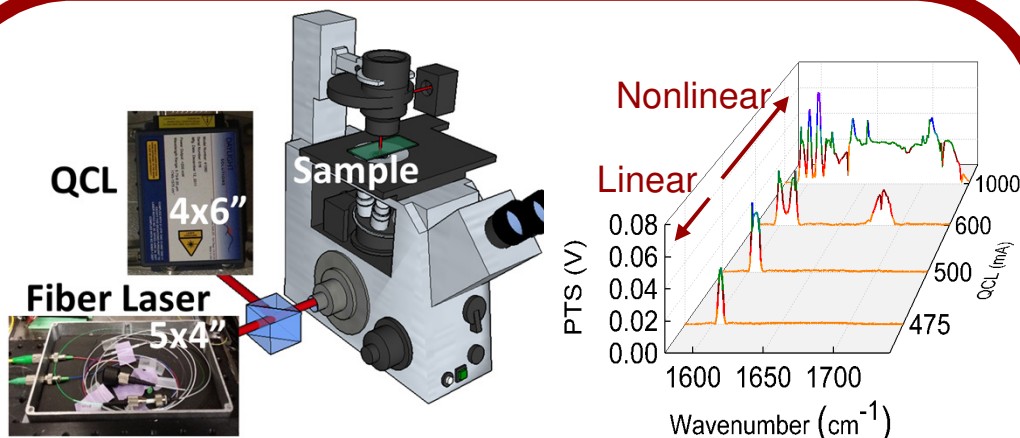


Infrared Nerve Stimulation: Temporal Pulse Shaping and Hybrid Wavelengths

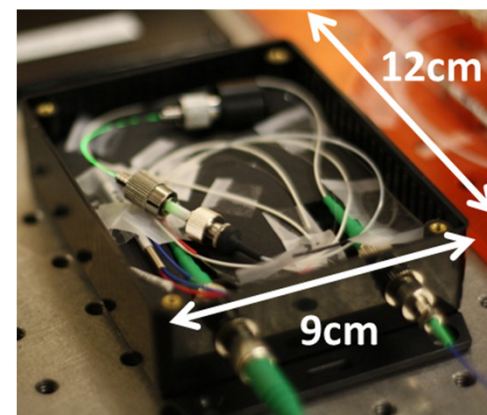


- Monitor and understand fundamental biophysical phenomena and cell membrane dynamics induced by infrared nerve stimulation
- Novel characterization methods and enhancement of infrared nerve stimulation based on customized laser operating parameters

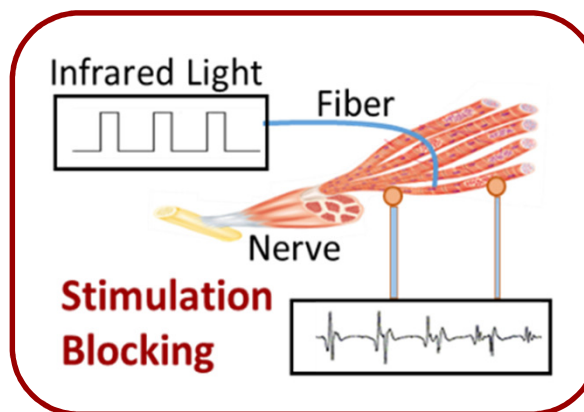
Approach



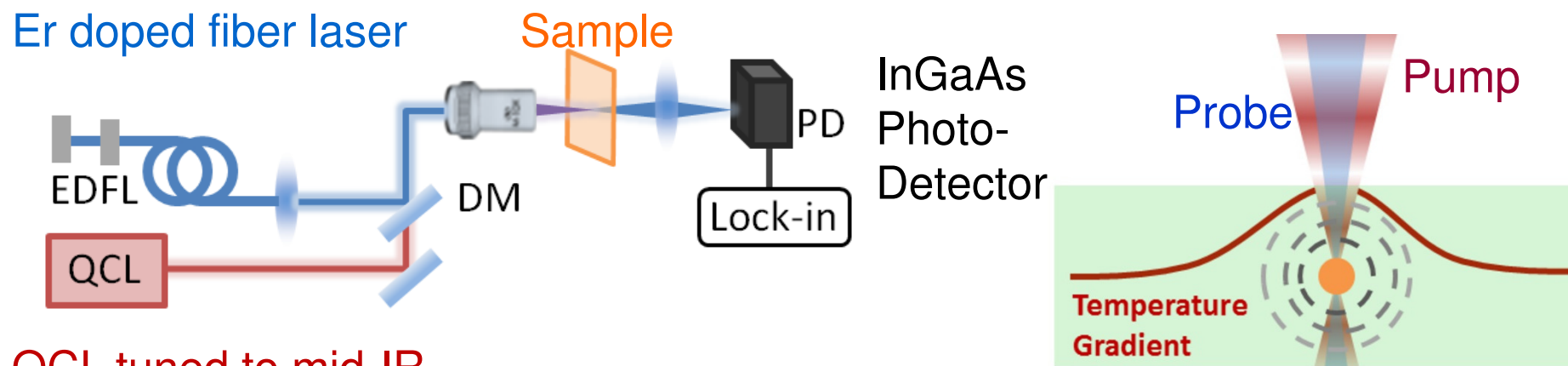
Label-free nonlinear photothermal spectroscopy sensitive to phase transition and structure, protein and lipid bilayers dynamics



Customized Tm fiber lasers ($1.8 - 2.1 \mu\text{m}$): Novel pulse dynamics and hybrid λ excitation



Photothermal Spectroscopy

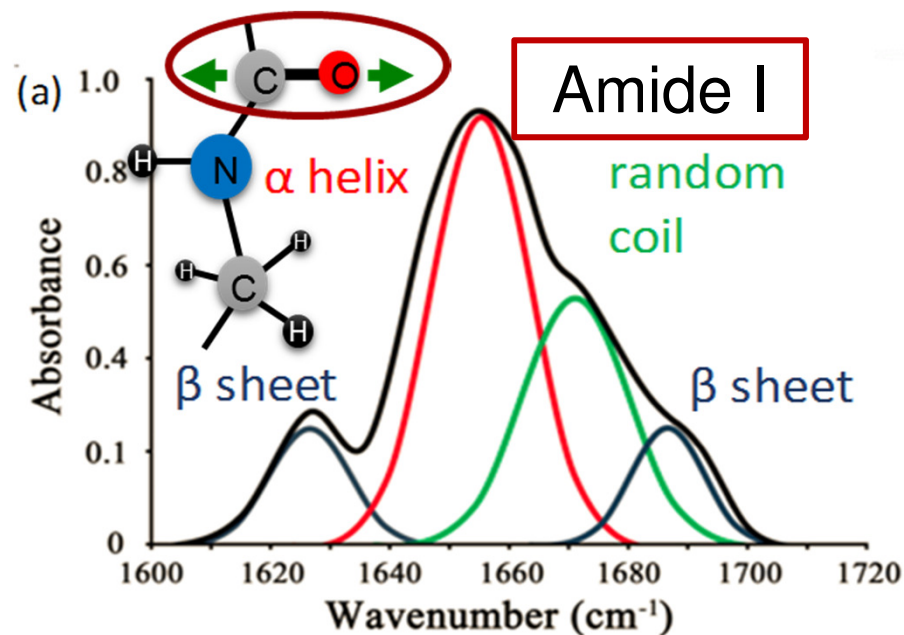
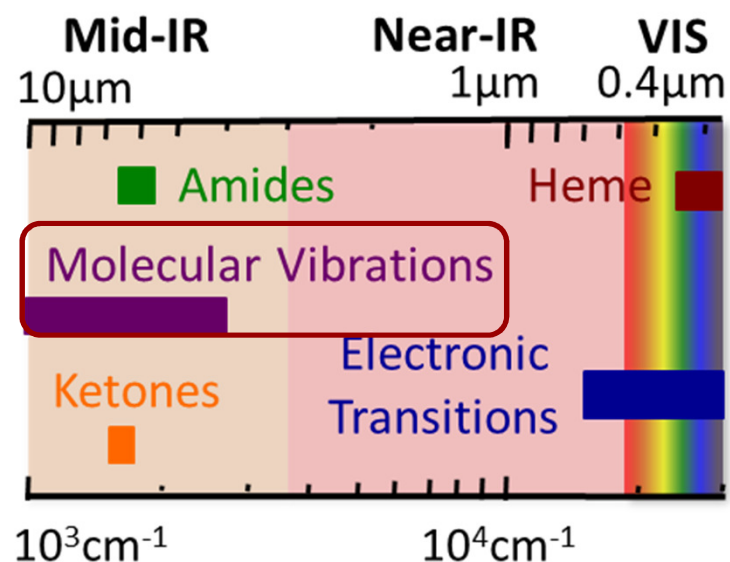


QCL tuned to mid-IR
absorption resonance

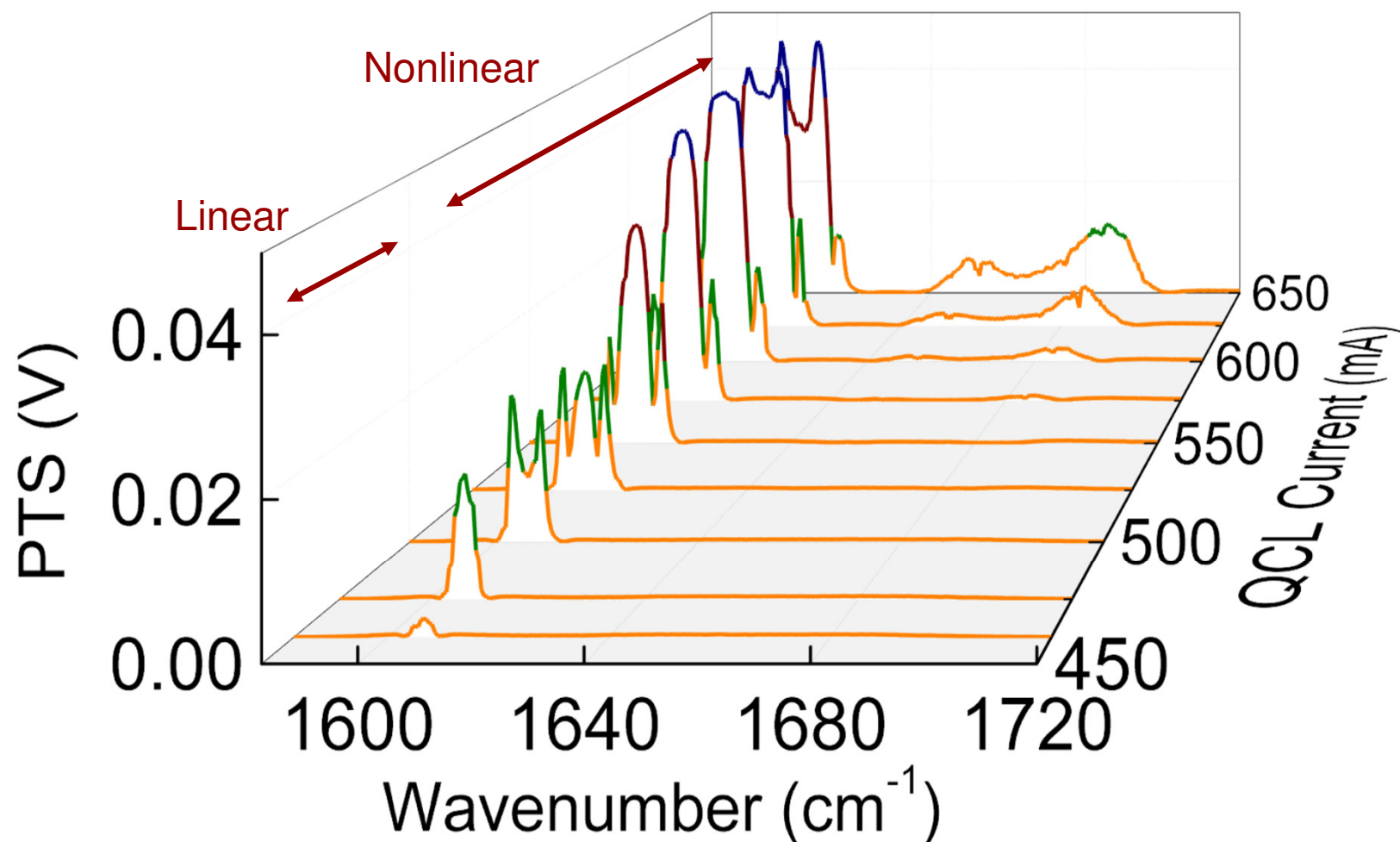
$$\Delta n = \frac{\partial n}{\partial T} \Delta T$$

- Absorbed pump power induces non-equilibrium state and localized sample heating
- Probe laser scatter detected in heterodyne measurement with lock-in technology
- Sub-diffraction limited spatial resolution

Label-Free Photothermal Imaging

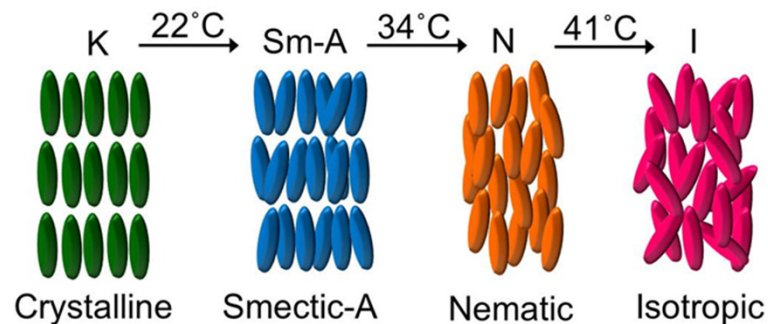


Nonlinear Spectroscopy

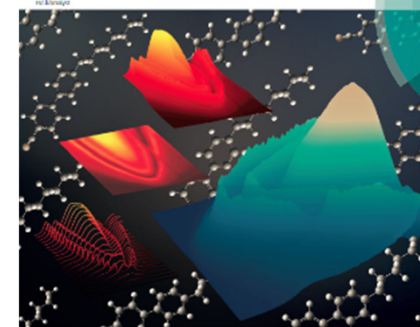


- Spectral narrowing/bifurcation and enhancement in nonlinear regime
- 4-Octyl-4'-Cyanobiphenyl (8CB): C=C stretching at 1607cm^{-2}

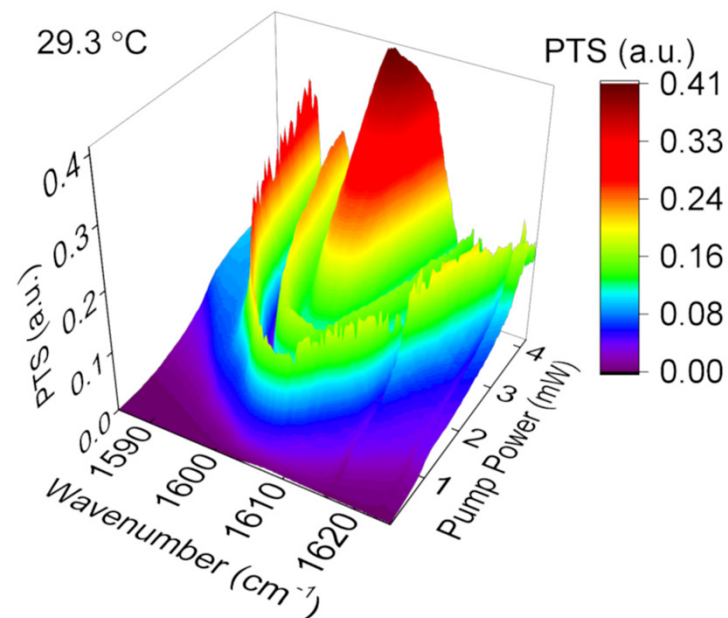
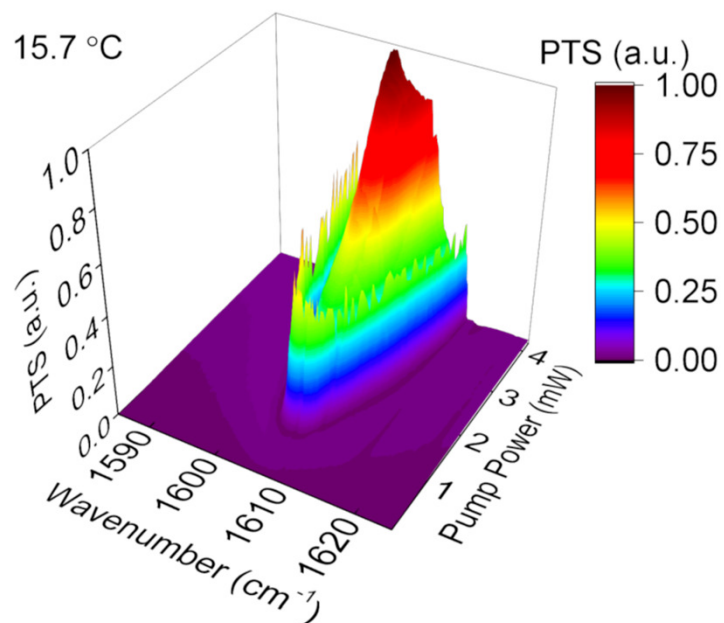
Different 8CB Phases



Analyst

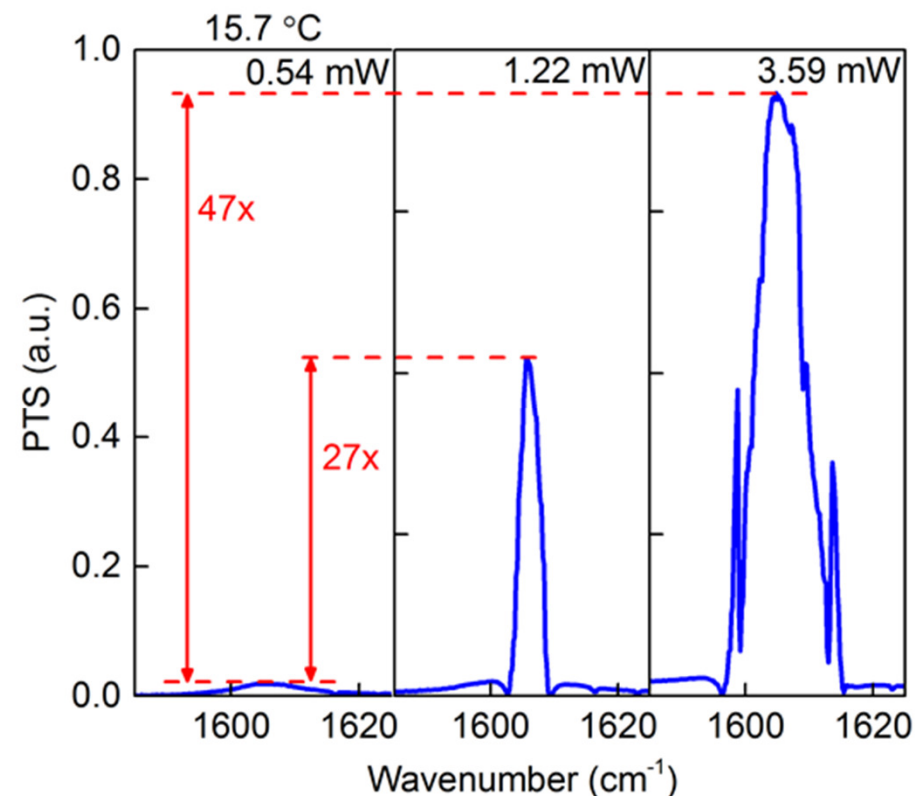
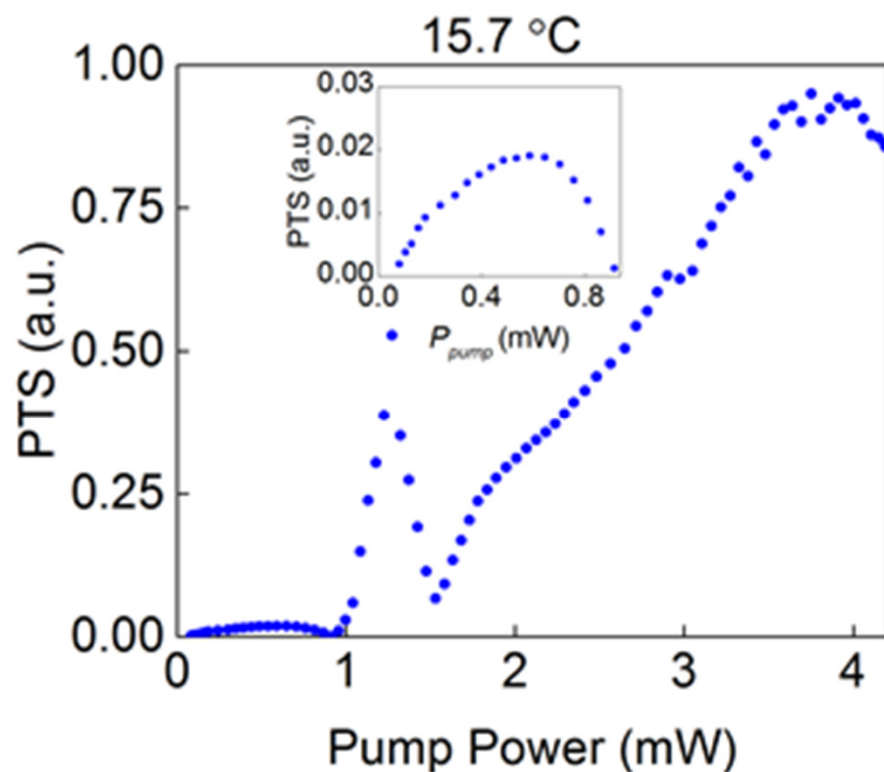


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Totachawattana, Analyst (2017)

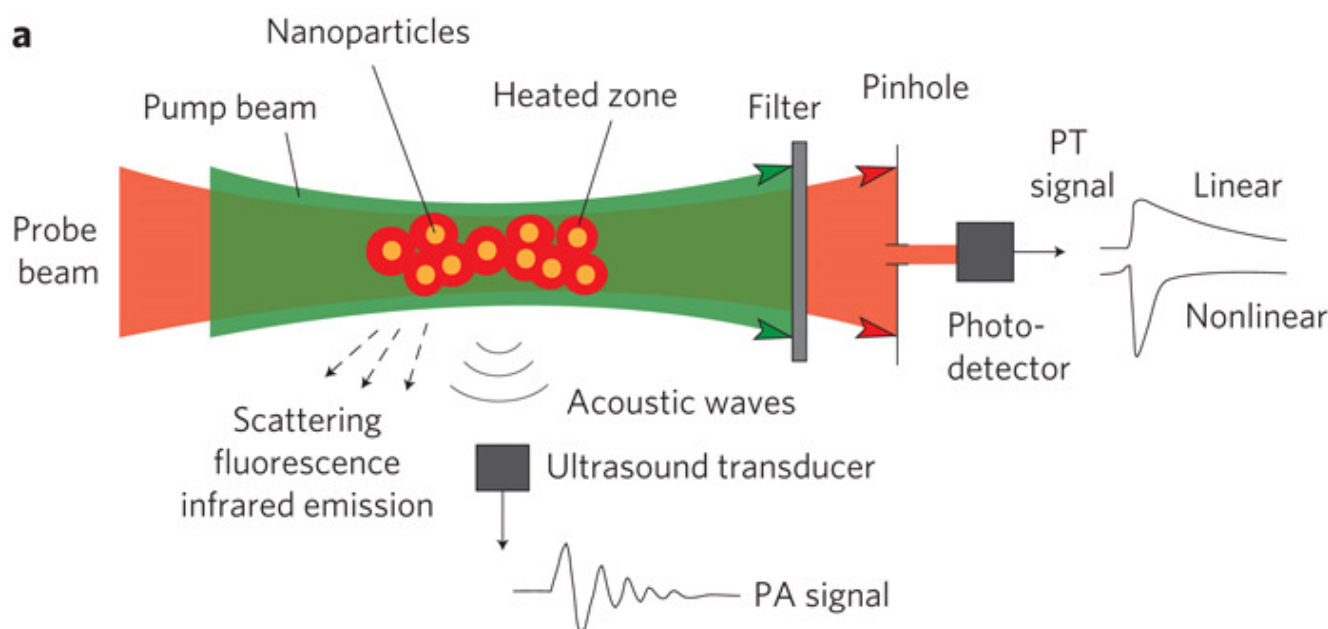
Nonlinear Signal Enhancement



- Largest increase at 1st enhancement: 27 x increase in signal by increasing pump power by 2.3 x
- ~47 x increase in signal strength for 6.6 x increase in pump power

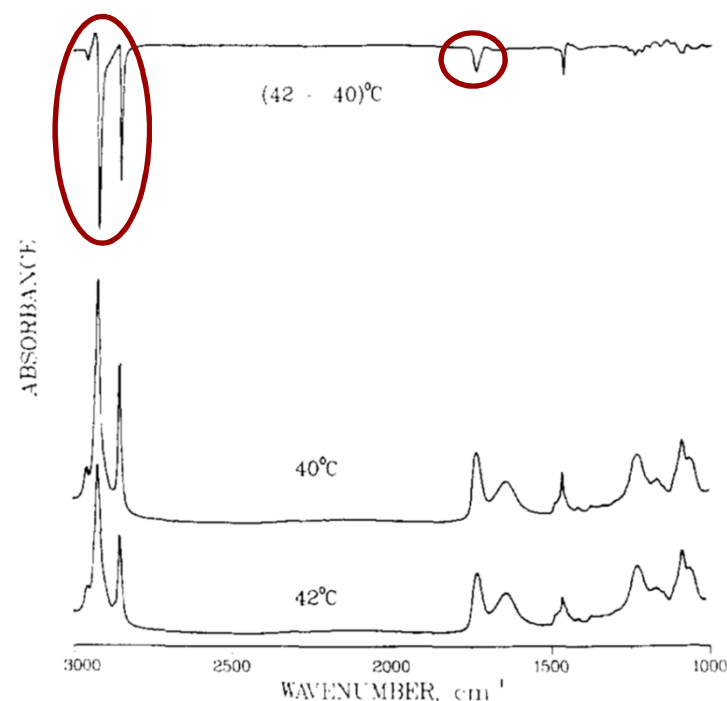
“Nanobubble Formation”

- Nanobubbles with distinct boundaries increase backscatter, reduce forward scatter



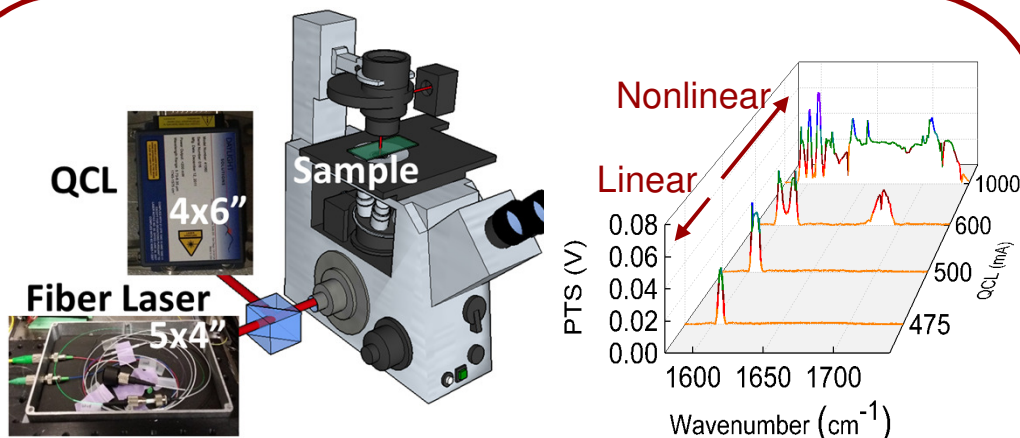
Phase Transitions in Artificial Lipid Bilayers

- Unilamellar Vesicles
- Phospholipids (DPPC with DSPE-PEG 2K)
- Measured C=O stretching band around 1735cm^{-2}

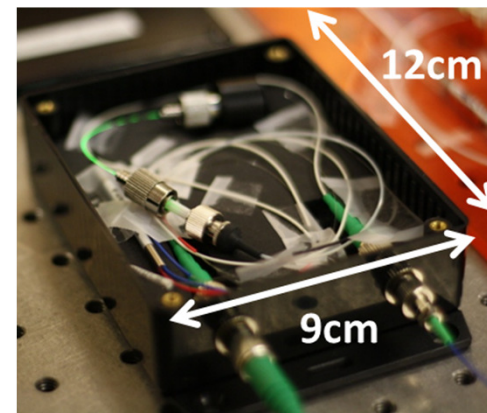


Casal, Biochimica, 1984

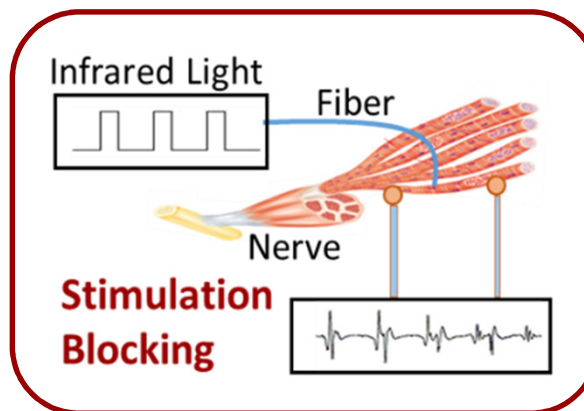
Collaboration: Dr. Tyrone Porter, BU Mechanical Engineering



Label-free nonlinear photothermal spectroscopy sensitive to phase transition and structure, protein and lipid bilayers dynamics

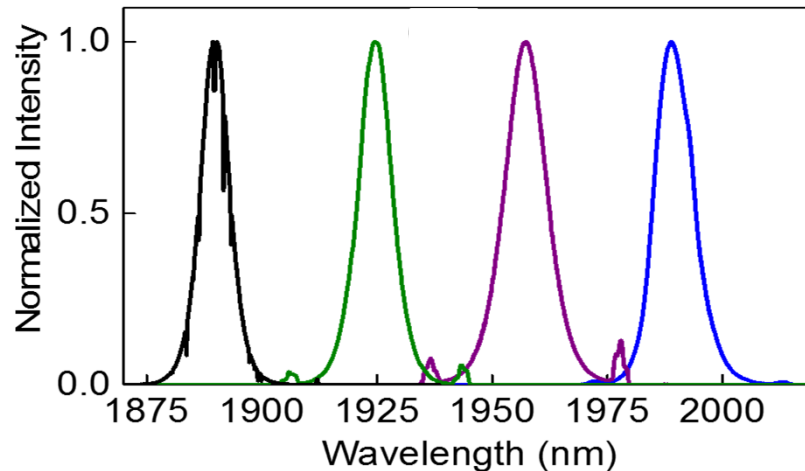


Customized Tm fiber lasers (1.8 – 2.1 μm): Novel pulse dynamics and hybrid λ excitation

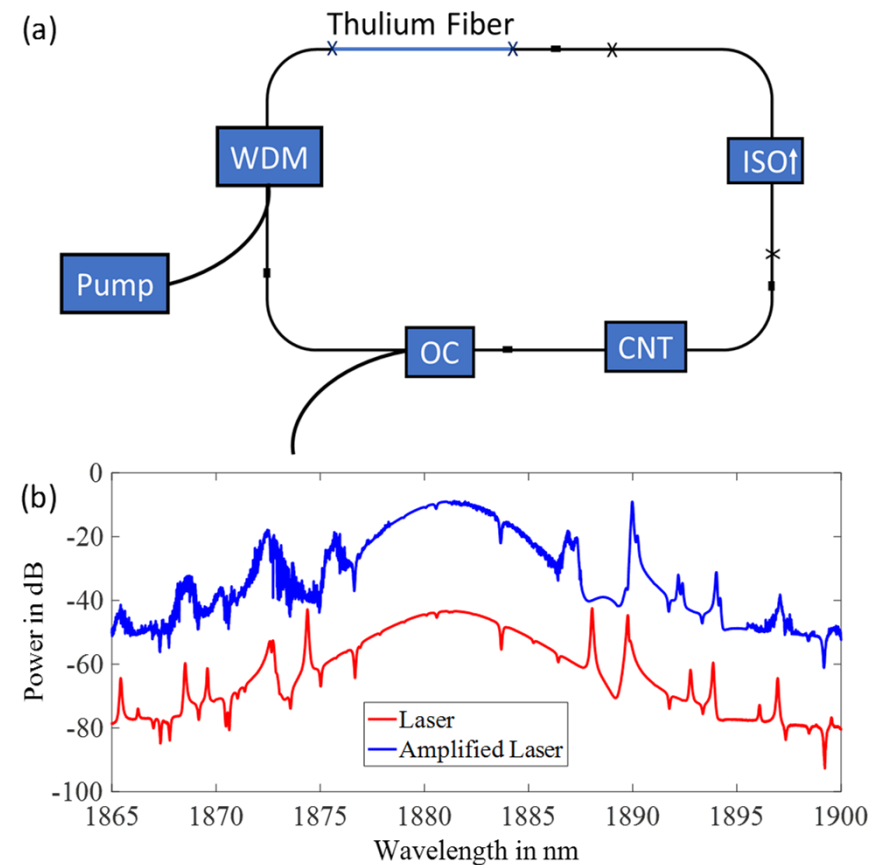


Thulium Fiber Laser

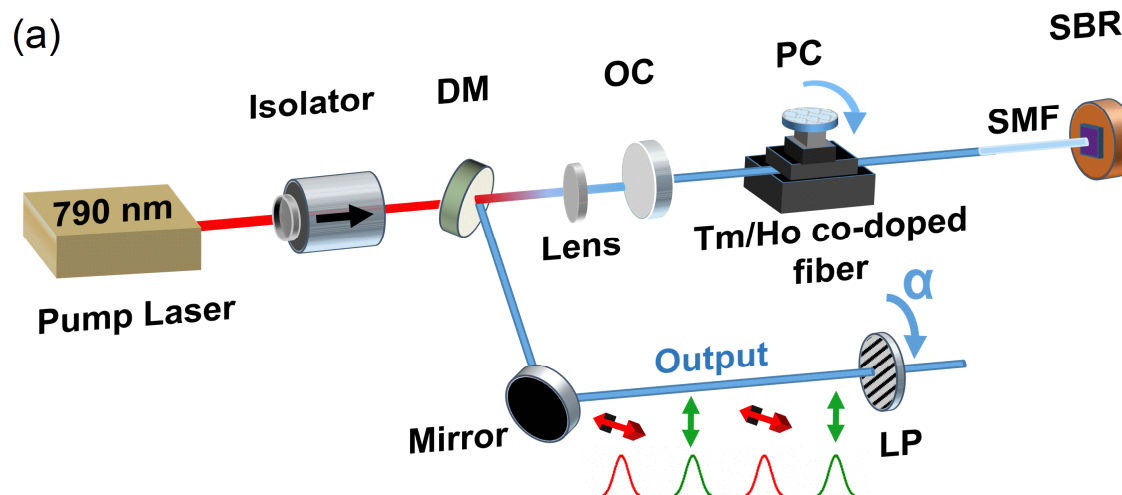
- Tunable cw thulium laser source



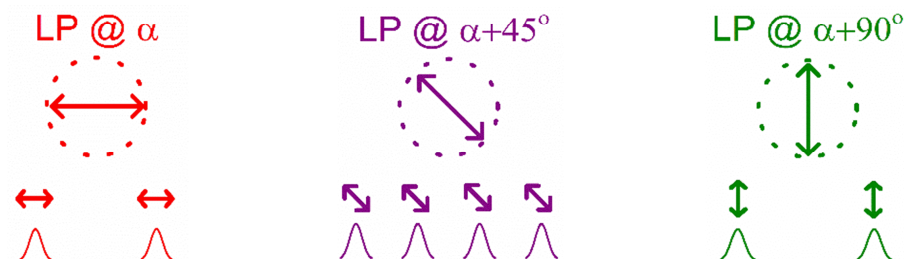
- Ultrafast thulium laser source
- repetition rate of 20.5 MHz
- center wavelength of 1882 nm
- ~ 930 fs pulse duration
- single-mode fiber



Polarization Vector Solitons

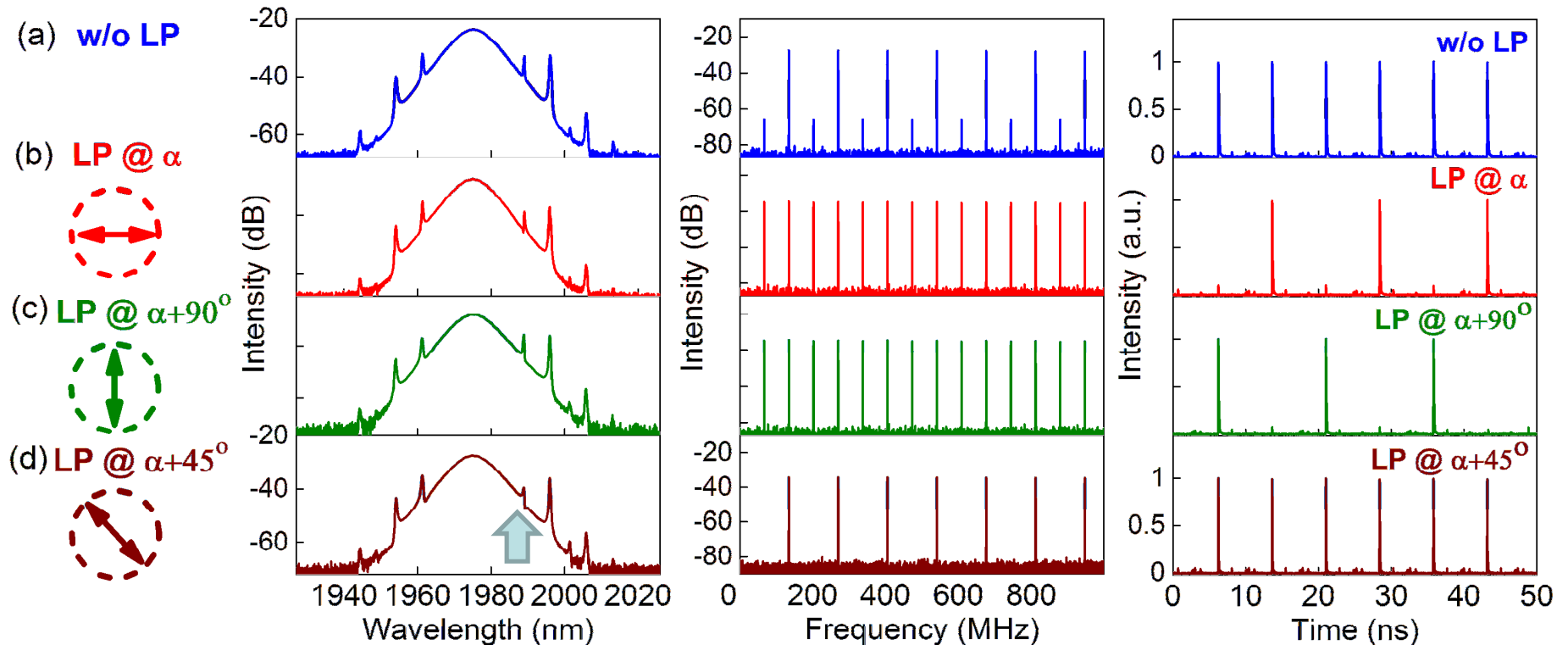


(b) Polarization Resolved Characterization



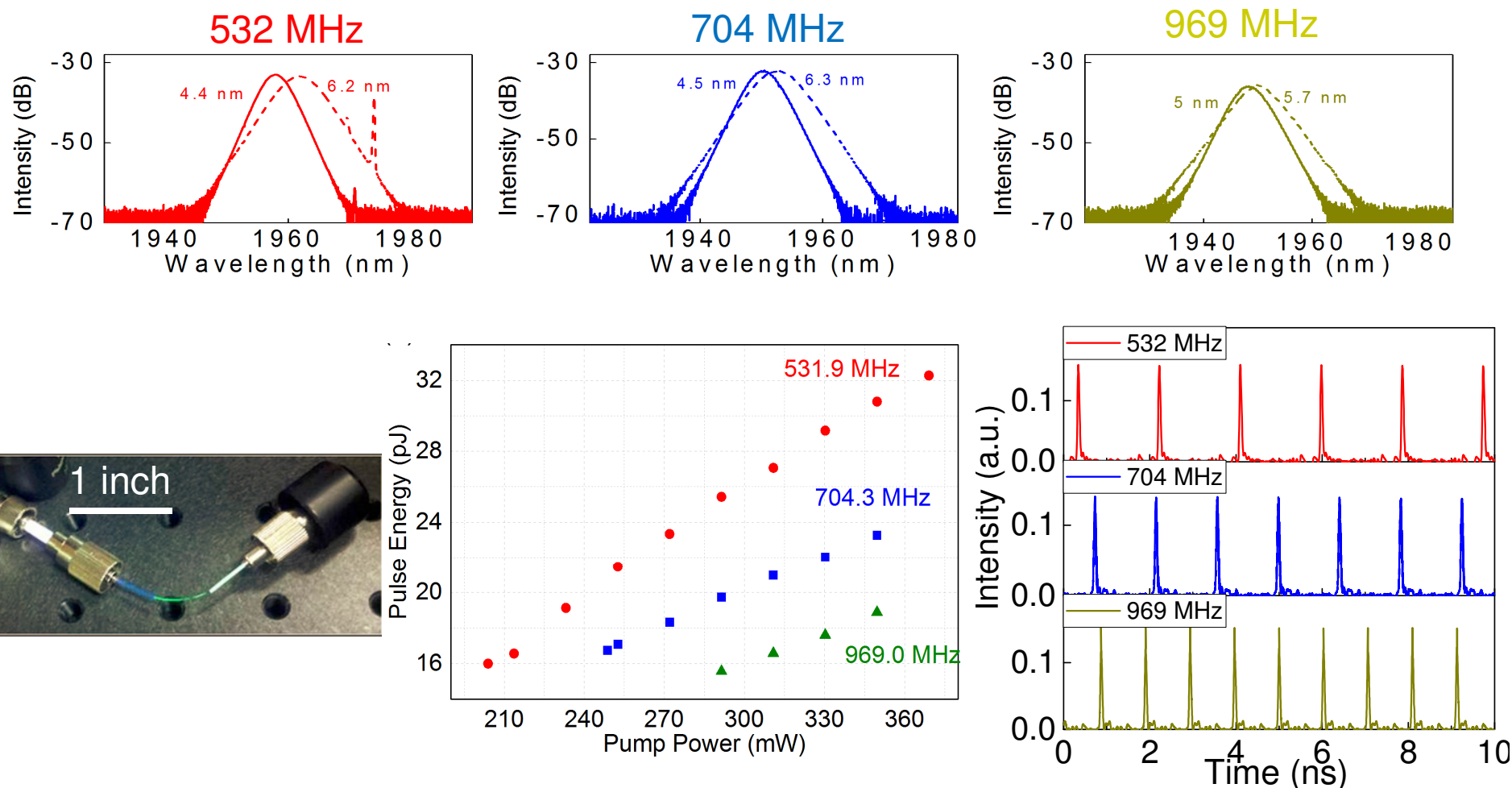
- Rotating polarization ellipse at output
- Novel states with coherent energy exchange

Novel Interlaced Pulse Train

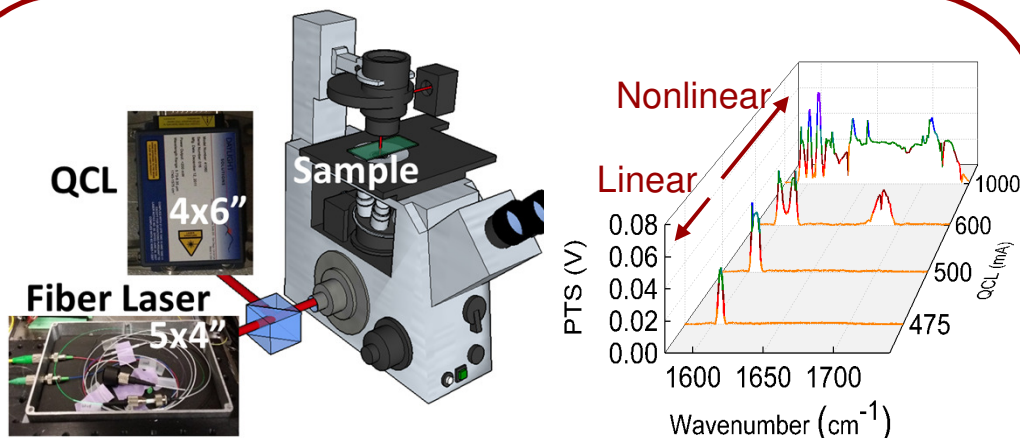


- orthogonal eigenstates are separated with an external linear polarizer
- co-generated, equal intensity and orthogonally polarized interlaced pulses
- four-wave mixing/ coherent energy exchange

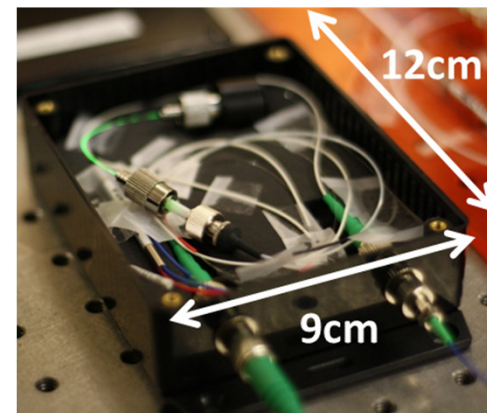
Towards GHz Repetition Rate



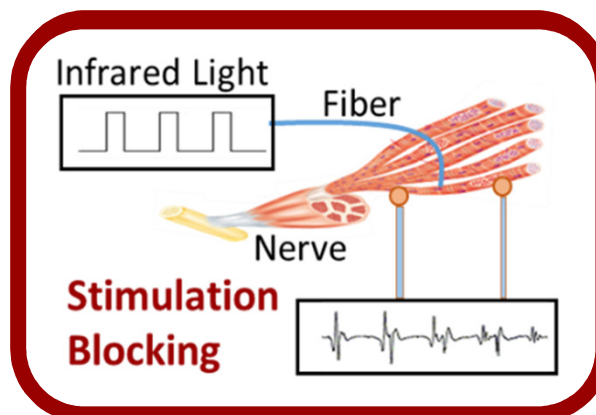
- Center wavelength from 1957 nm to 1962 nm
- Average output power from 7.1 mW to 13.8 mW



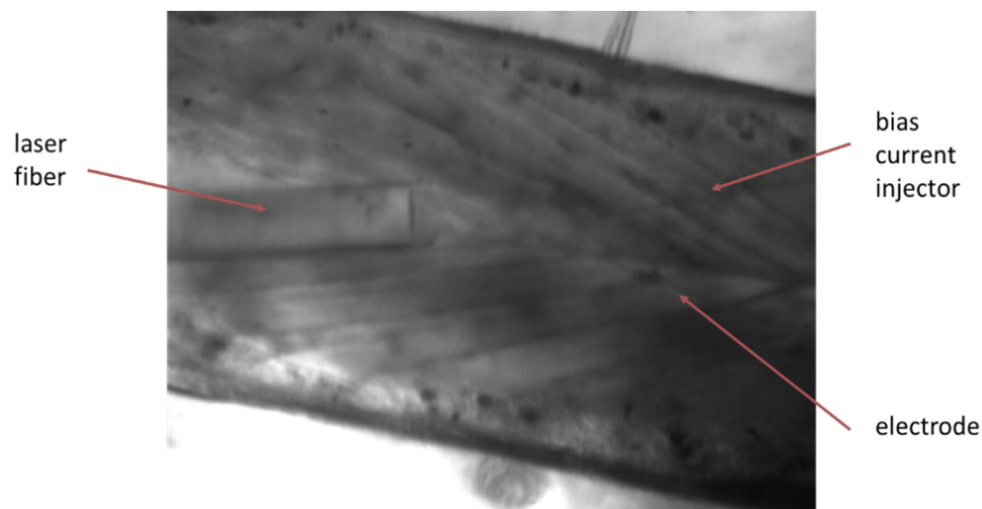
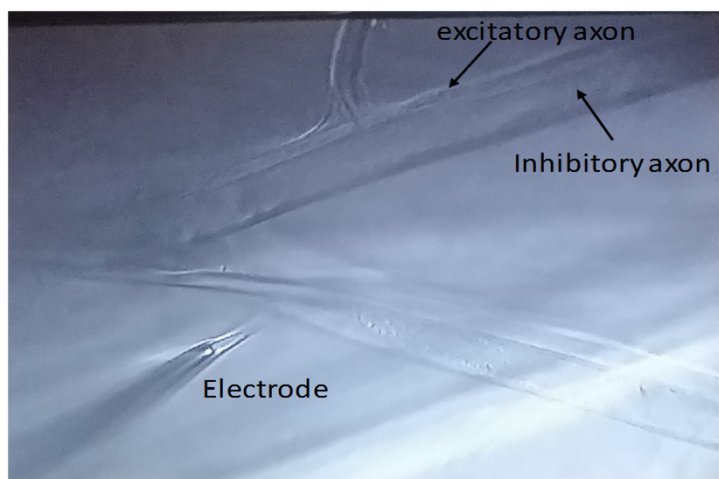
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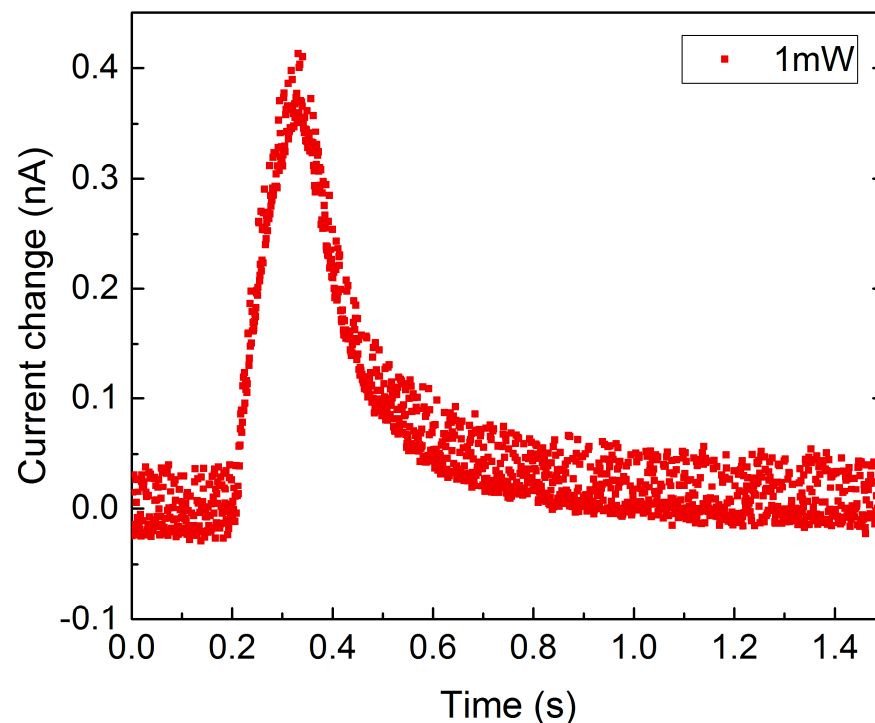
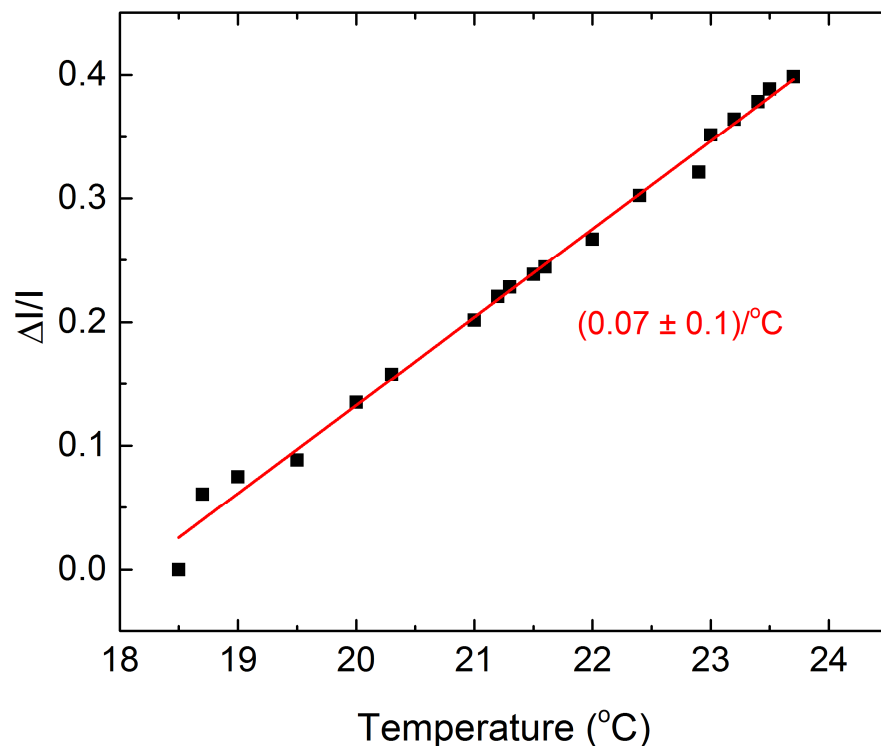
Crayfish Walking Leg: Opener Neuromuscular Junction



- unmyelinated axons, morphologically similar to branching axons in mammalian CNS
- encased in glia cells
- two axons are excitatory and inhibitory in function with glutamate and GABA as neurotransmitters, innervate ~100 muscle fibers

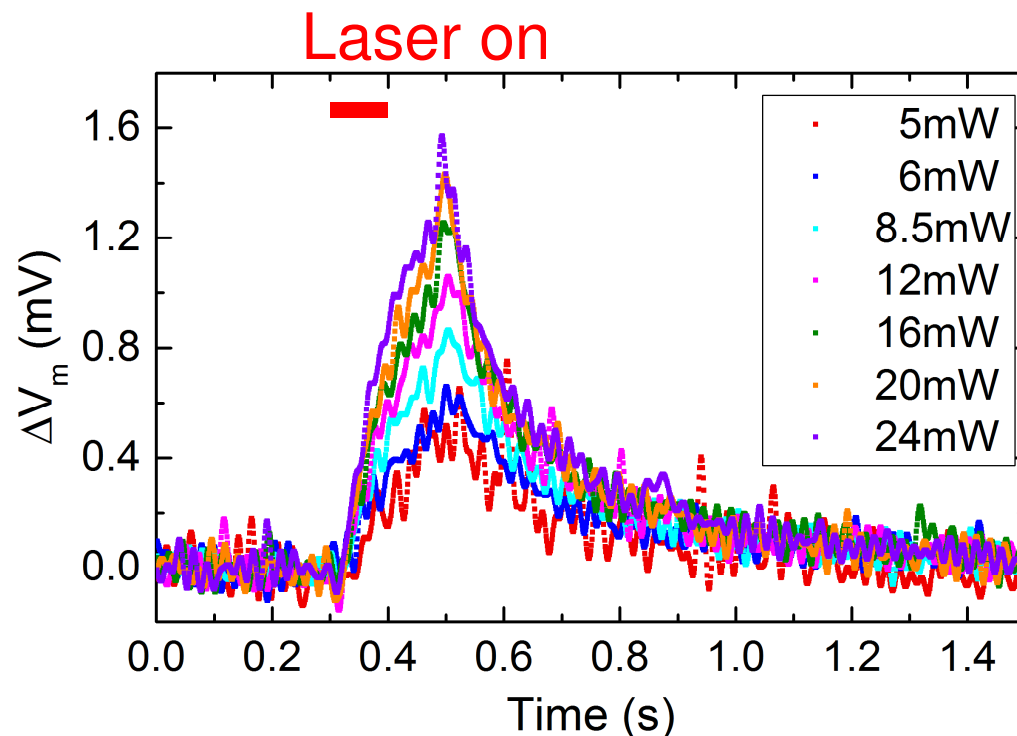
Collaborator: Dr. Jen-Wei Lin, BU Biology

Patch Clamp Temperature Calibration



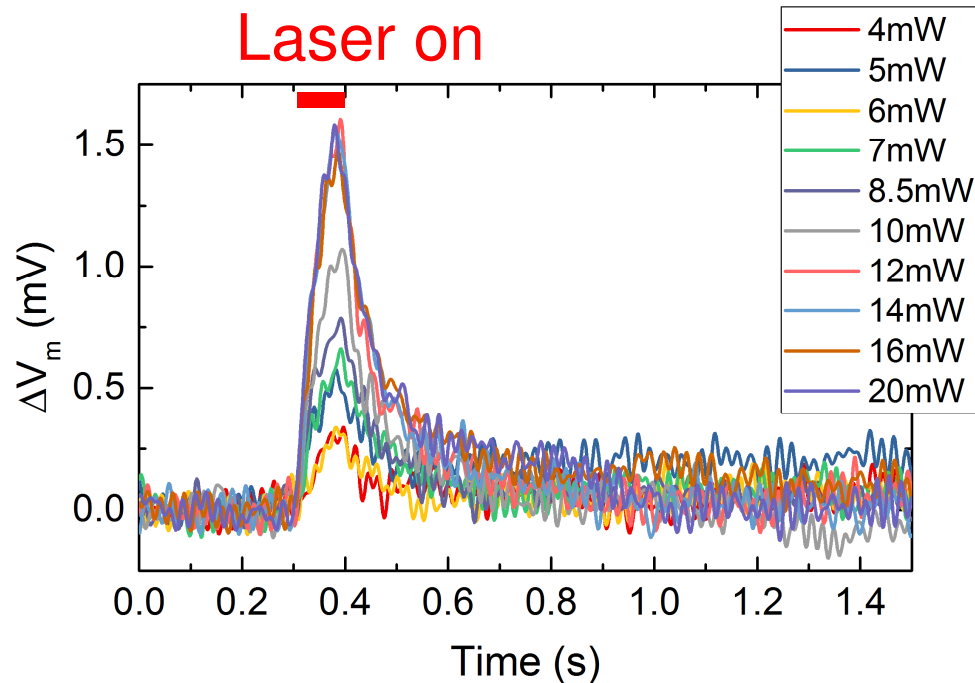
- Temperature measurements with 50 μm core diameter fiber in saline bath
- Current change for 1mW (100 ms) corresponds to $\sim 2.5^{\circ}\text{C}$ temperature change

Muscle Fiber Stimulation



- 50 μ m core size and 100ms pulse duration,
- Rise time to peak \sim 200ms, relaxation \sim 400ms

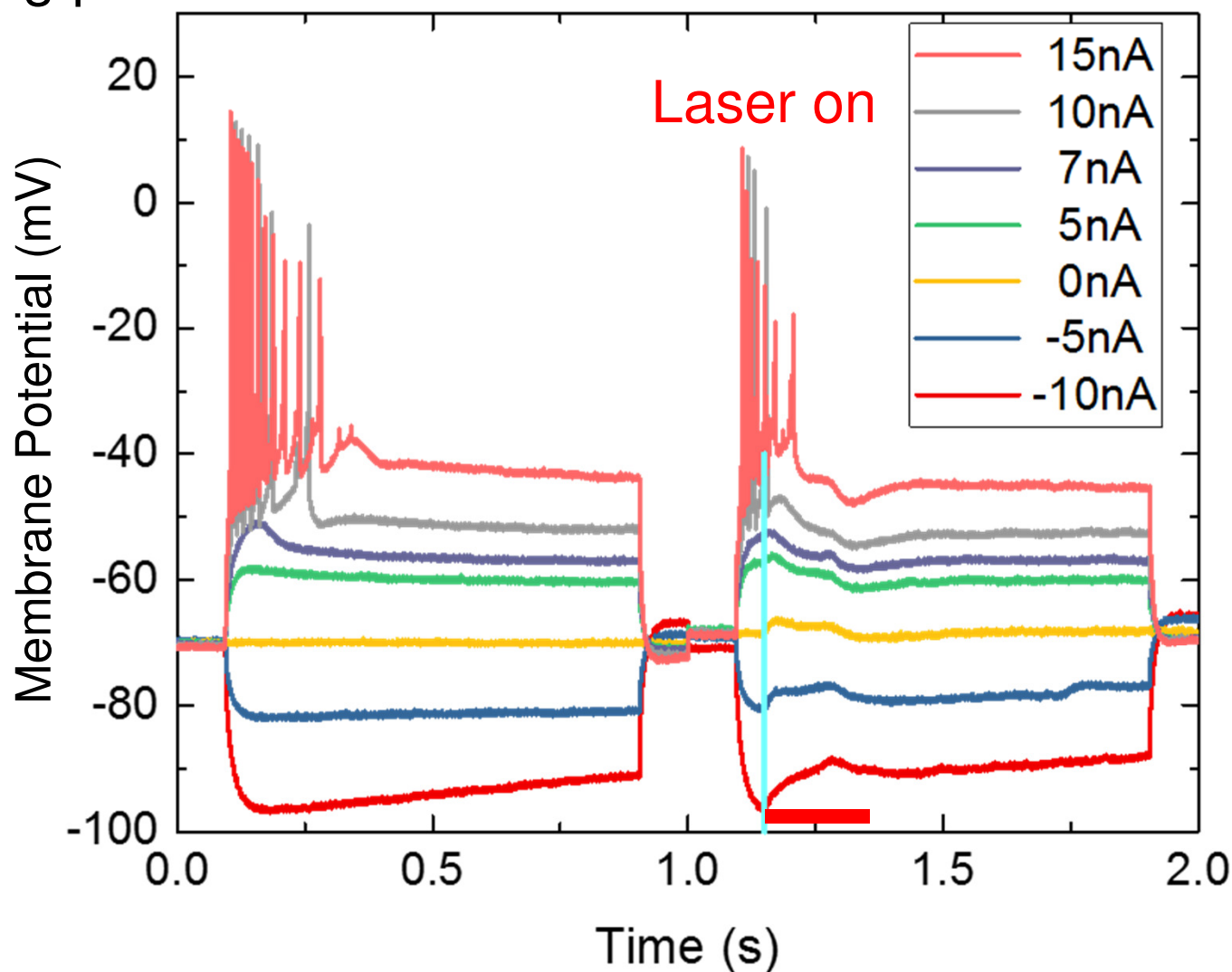
Single-Mode Fiber



- Single-mode fiber with a mode-field diameter of 13 μ m
- Faster rise time to peak ~ 90 ms corresponding to applied pulse duration, relaxation ~ 200 ms

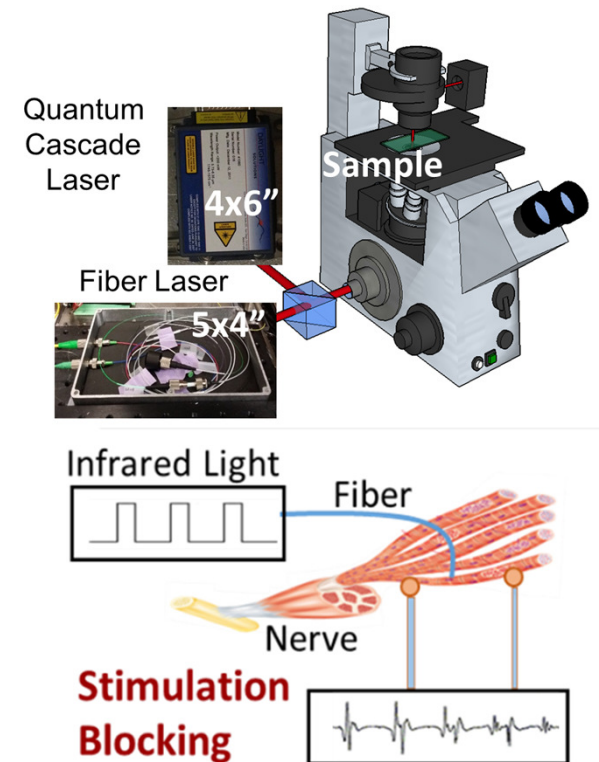
Action Potential Blocking

Study of axonal excitability and inhibition for different holding potential



Summary

- Novel pulsing regimes and photothermal spectroscopy to study cell membrane dynamics and underlying biophysical cellular mechanisms during infrared nerve stimulation



Dr. Sofi Bin-Salamon

We have open positions for a post-doc and PhD students

