Rockwell Laser Industries Presents

Nonlinear Processes in Threshold Damage to Tissues Relevant to Laser Safety

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1

Presenter's Credentials

- Bachelors of Science in Physics; Doctorate in Physics
- National Academy of Science/ National Research Council (NRC) Postdoctoral Associate, Brooks Air Force Base, Texas (2 years)
- Laser Safety Analysis and Training- Rockwell Laser Industries since 1998
- Research Physicist for Air Force Research Laboratory (30 years)
  - Focus on bioeffects of ultrashort laser exposures to eye and skin
  - Representative to national and international laser safety standards committees
- Fellow of AFRL, Fellow of SPIE, Fellow of LIA
- Active in National and International Laser Safety Standards Consensus Standards

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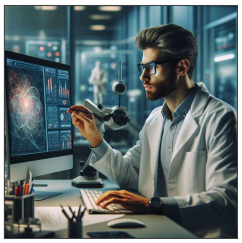
Laser Bioeffects Knowledge …

- Informs Risk Analysis (Severity of Injury, Probability of Over-Exposure)
- Laser Bioeffects Underpin the ANSI, ACGIH, and ICNIRP Safe-Exposure Limits
  - Provides Understanding for Correction Factors, Variation in MPE
  - Assists in Evaluation of Accidental Over-Exposures
  - Informs Management Decisions on Laser Worker Medical Surveillance
- Assists in Determination of When No Risk Exists from Laser Exposure
- Part of Large Application Area of Medical Applications of Laser Exposure- NOTE: Not Intent of This Talk
  - Skin Rejuvenation, Tattoo Removal, Tissue/Disease Spectroscopy, Surgery



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Outline

- Overview of linear/ thermal threshold injury to retina
- Types of nonlinear bioeffects mechanisms
  - Phase change- microcavitation
  - Nonlinear optical
    - Self-focusing
    - Supercontinuum generation
- Summary and Conclusions

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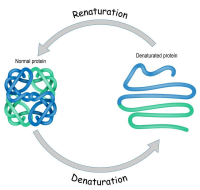
4- Step Process of Thermally Denaturing a Protein

- **Absorption of Thermal Energy**: Laser energy is absorbed in a chromophore, most likely melanin granule for retina or skin, and local temperature rises. This disrupts the **hydrogen bonds** and **hydrophobic interactions** in nearby proteins that maintain the secondary (alpha-helices/beta-sheets) and tertiary structures.
- **Unfolding**: The protein loses its compact, "native" conformation. It transitions into a disordered, "random coil" state. While the 3D shape is lost, the **primary structure** (the sequence of amino acids held by strong peptide bonds) typically remains intact.
- **Exposure of Hydrophobic Groups**: Proteins are usually folded so that hydrophobic parts are tucked inside. Denaturation flips these groups outward, making the protein insoluble in water.
- **Aggregation and Coagulation**: The exposed hydrophobic regions of different unfolded proteins stick to each other. This creates large, tangled clumps—a process you see visually when an **egg white turns from clear to opaque** while frying.



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When done quickly and to moderate temperatures, as in a retinal lesion, the tissue does not renature (non-reversible process).

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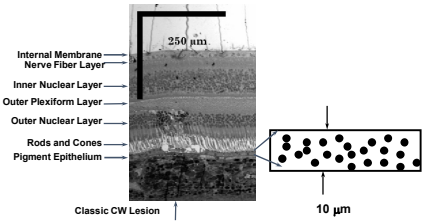
The Retina



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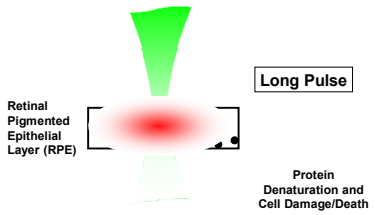
Traditional Thermal Understanding



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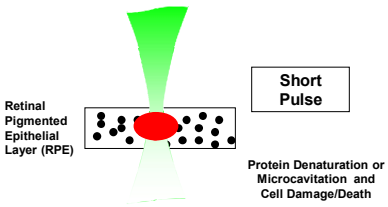
Thermal Damage - Short Pulse



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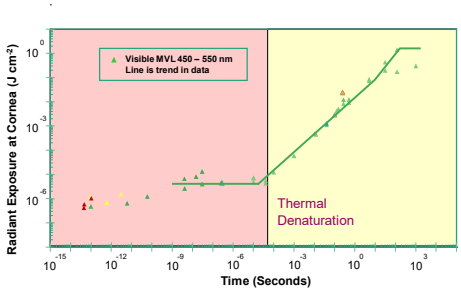
Retinal Lesion Mechanisms for Damage



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Nonlinear Mechanism 1
Phase Change

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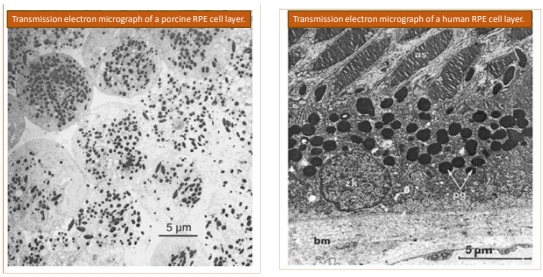
Melanin in a Retinal Pigmented Epithelium Cell



Ralf Brinkmann, Gereon Huttmann, Jan Rogener, Johann Roider, Reginald Birngruber and Charles P. Lin, "Origin of Retinal Pigment Epithelium Cell Damage by Pulsed Laser Irradiance in the Nanosecond to Microsecond Time Regimen", Lasers in Surgery and Medicine 27:451–464 (2000).

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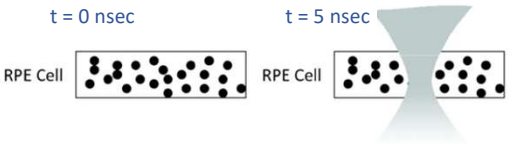
Microcavitation Process



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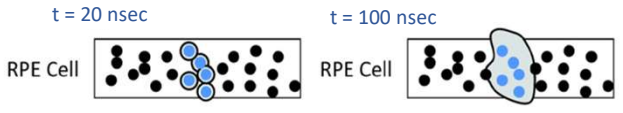
Microcavitation Process



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Microcavitation Process

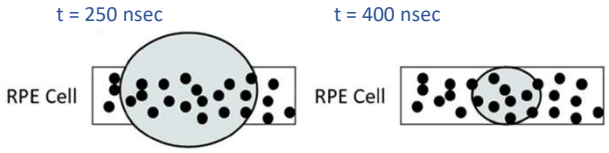

Figure adapted from: B.A. Rockwell, R.J. Thomas and A. Vogel, "Ultrashort laser Pulse Retinal Damage Mechanisms and Their Impact on Thresholds", Medical Laser Appl. 25(2), 84-92 (2010).

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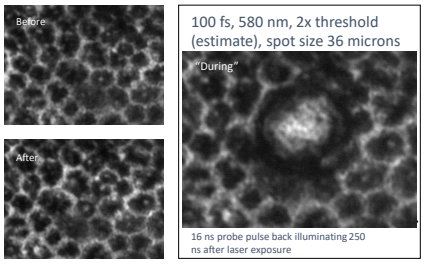
Ex-vivo Cells and Pump-Probe Microscopic Photography



C. P. Lin and M. W. Kelly, "Ultrafast time-resolved imaging of stress transient and cavitation from short pulsed laser irradiated melanin particles," SPIE *Laser-Tissue Interactions VI, Proc. SPIE* 2391, 294-299 (1995).

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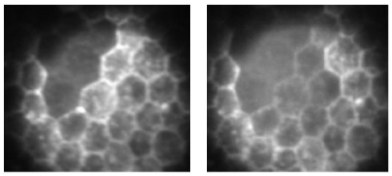
Viability Assay on Ex Vivo RPE Cells



Before laser exposure Post laser exposure

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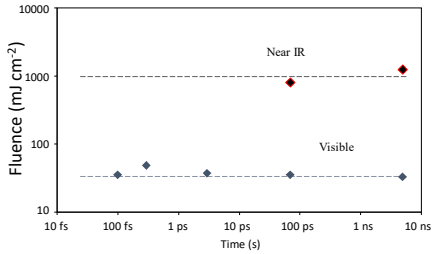
Microcavitation Thresholds for the Rabbit RPE Layer



D. J. Payne, J. J. Elliot, B. G. Eilert,G. D. Noojin, R. A. Hopkins Jr., C. P. Lin, B. A. Rockwell, "Cavitation thresholds in the rabbit retinal pigmented epithelium", in Laser-Tissue Interaction X , Steven L. Jacques, Ed., Proc. SPIE Vol. **3601**, 27-31 (1999).

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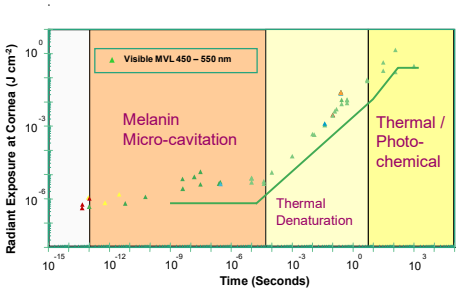
17

Retinal Lesion Mechanisms for Damage



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Nonlinear Mechanism 2
Self-Focusing (Nonlinear Optical)

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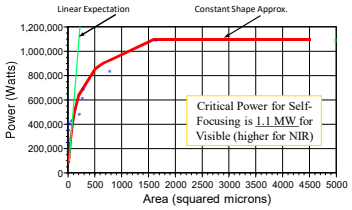
Measurement of Self-focusing

- Irradiance would destroy knife-blade at self-focused powers
- Used LIB threshold to show irradiance enhancement



Soileau MJ, Williams WE, Mansour N, Van Stryland, EW. Laser-induced damage and the role of self-focusing. Opt Eng 1989;28(10):1133–44.

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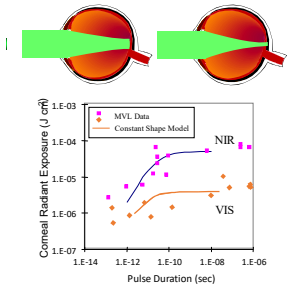
NLO Hypothesis



- Self-focusing phenomena decreases the MVL threshold for Visible and Near-Infrared Wavelengths for pulse widths shorter than 10 ps
  - Calculations to determine onset of phenomena
  - In-vitro and Ex-vivo measurements discount possible involvement of RPE photoacoustics

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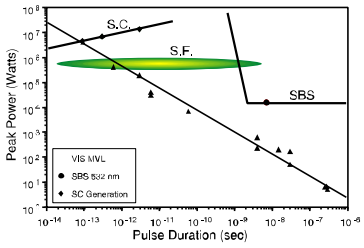
NLO Effects on MVL Thresholds



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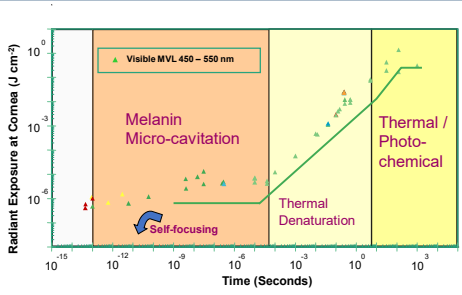
Retinal Lesion Mechanisms for Damage



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Additional Known Non-Linear Optical Effects

- Laser-induced breakdown (LIB)
  - Measured in artificial eyes, well characterized
  - Shown in histopathology studies to be mechanism of threshold damage for 100 fs pulses
  - Can be used to estimate retinal spot sizes
- Supercontinuum generation
  - Measured to be suprathreshold phenomena for visible to 1064 nm
  - Recently studied in 1300-1400 nm range for 100 fs-10 ps to be relevant to reduce threshold damage level

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Summary and Conclusions

- Understanding the mechanisms of tissue damage for 10^{-14} to 10^{3} sec for 180 nm to 1,000,000 nm is complex
- Understanding thermal damage is critical
- Novel non-linear effects provide unique reduction of damage thresholds by up to 1000x

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Questions

Laser Induced Breakdown

Self focusing

Stimulated Brillion scattering

supercontinuum

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26

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27