Light scattering methods for tissue diagnostics

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INTRODUCTION TO LIGHT SCATTERING

- Light scattering has emerged as a vital tool in biomedical research, enabling diagnostic sensitivity to a variety of tissue alterations associated with diseases.

- The interactions between light and tissue are particularly attractive for diagnostics due to the diverse contrast mechanisms available, including: Spectral Analysis, Angle-Resolved Detection, Fourier-Domain Detection.

- Photonic diagnostic tools offer several advantages: Non-Ionizing, Non-Invasive, Real-Time Feedback.

PROBLEMS:
1. Complexity of Biological Tissues

- Heterogeneity at Multiple Scales
- Disorder vs. Organization
- Impact on Diagnostic Accuracy

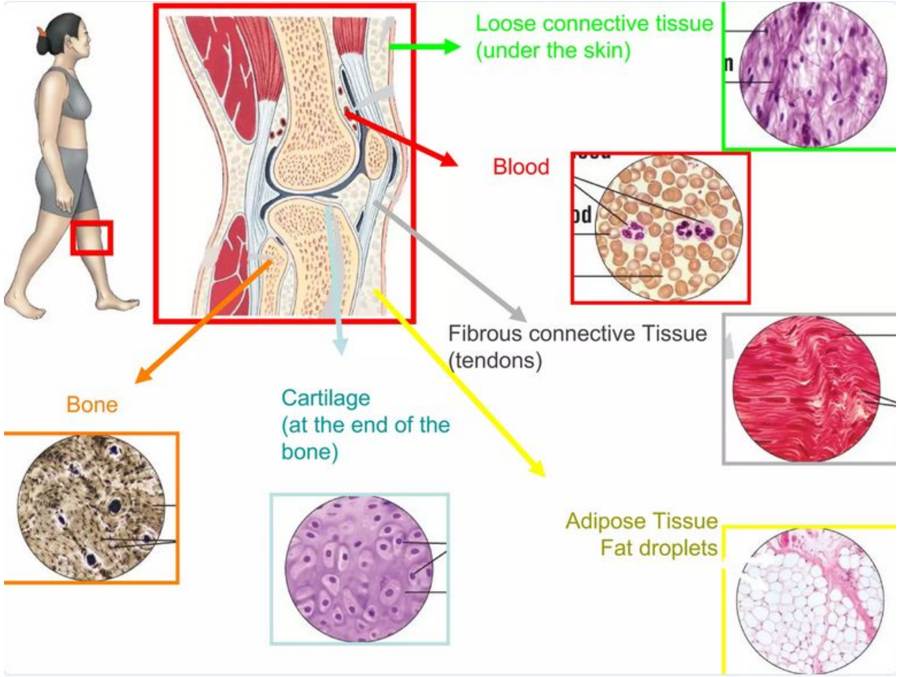


Fig 1: Illustration of connective tissues.
Credit: Kareen Martin [https://www.slideshare.net/slideshow/chapter-11-10066866/10066866]

PROBLEMS:
2. Inverse Problems:

- Difficulty in Unique Solutions
- Measurement Limitations
- Need for Advanced Models
- Regularization Techniques

PROBLEMS:
3. Need for Effective Diagnostic Tools

- Non-Invasive Techniques Required
- Challenges in Current Methods
- Integration of Multiple Parameters
- Clinical Relevance

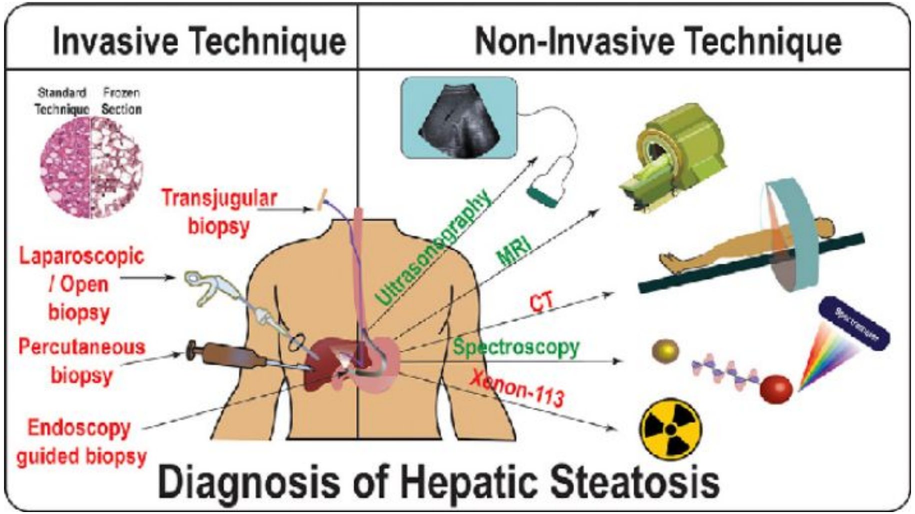


Fig 2: Illustration of invasive and non-invasive technique available for the diagnosis of Hepatic steatosis.
Credit: Allwyn S Rajamani [Allwyn S. Rajamani et al. (2022)]

Wavelength-Dependent Light Scattering
1. Elastic-Scattering Spectroscopy (ESS)

- A non-invasive optical technique that analyzes the spectrum of diffuse scattering from tissues for clinical diagnostic purposes.

- Breast Cancer, Colonic Lesions, Barrett's Esophagus

- Spectral analysis in ESS can take many forms:
  - Direct analysis
  - Machine learning algorithms
  - Extraction of tissue optical properties

- Recent Developments:
  Discriminating benign from malignant disease in ex vivo thyroid samples

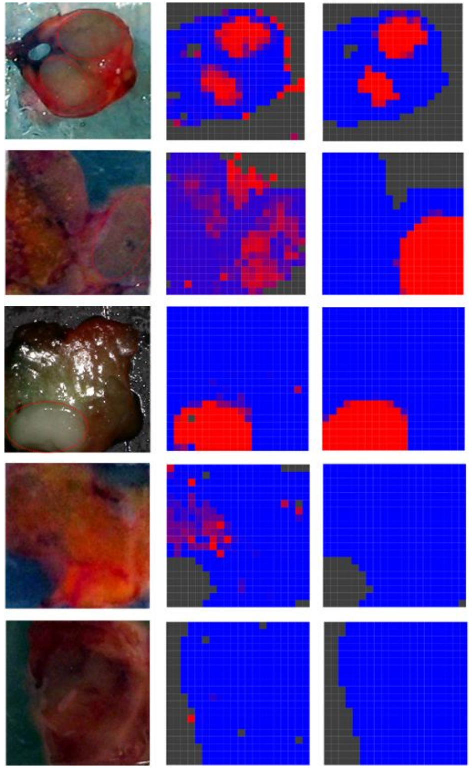


Fig 3: Examples of the constructed images from three partially or totally metastatic nodes (first, second, and third rows) and two totally normal nodes (fourth and fifth rows) using the two-stage image classification model in a reduced two-dimensional space. [Zhu Ying et al. (2018)]

Wavelength-Dependent Light Scattering
1. Elastic-Scattering Spectroscopy (ESS)

Light-Scattering Spectroscopy (LSS):

- An optical technique, related to ESS, that analyzes the spectrum of scattered light to determine the morphological properties of tissues.
- Polarization-Gated Detection, Mie Theory Application
- Barrett's Esophagus, Pancreatic Lesions, General Oncology Applications
- Enhanced capabilities in endoscopic applications and improved diagnostic accuracy

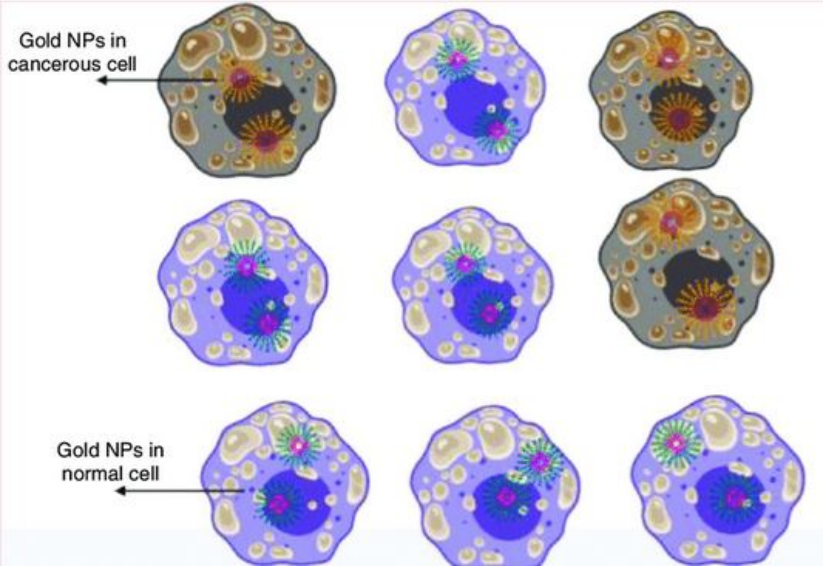


Fig 4: Light scattering and absorption spectra of cancer and normal cells attached with gold nanoparticle-conjugated anti-EGFR antibodies.
Credit: ResearchGate [Touqeer Ahmad et al. (2020)]

Wavelength-Dependent Light Scattering
2. Diffuse Reflectance Modeling

- It analyzes the light that is diffusely reflected from biological tissues to extract diagnostic information.
- Hemoglobin Concentration, Hemoglobin Oxygen Saturation, Effective Scatterer Density and Size
- Potential in clinical diagnostics (differentiating between normal and adenomatous colon tissues)

- Monte Carlo Methods:
  - These methods provide semi-empirical approximations that can replace complex analytical solutions
- Two-Layer Models:
  - More realistic representation of biological tissues
- Phase Function Studies:
  - Describes how light is scattered at different angles
  - Influence on the model predictions

Wavelength-Dependent Light Scattering
3. Spectroscopic Optical Coherence Tomography (SOCT)

- Combines traditional optical coherence tomography (OCT) with spectral analysis
- Key techniques: Windowing Methods and Dual-Window Method
- Quantifying Burn Severity, Retinal Oximetry, Microvascular Mapping
- Recent innovations: Inverse Spectroscopic OCT (ISOCT), Applications in Oncology

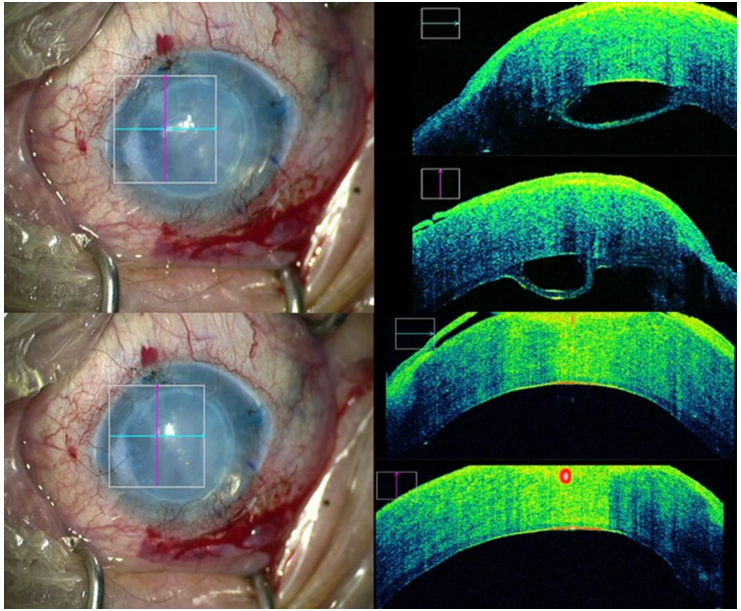


Fig 5: iOCT reveals an interface fluid [Marc B. Muijzer et al. (2021)]

Wavelength-Dependent Light Scattering
4. Dark-Field Spectral Scatter Imaging

- Microscopy technique that analyzes the spectral properties of scattered light from resected tissues while minimizing the contribution of specular reflections.
- Significant promise in assessing breast surgical margins
- Accurate spectral analysis and the ability to rapidly analyze tissue samples

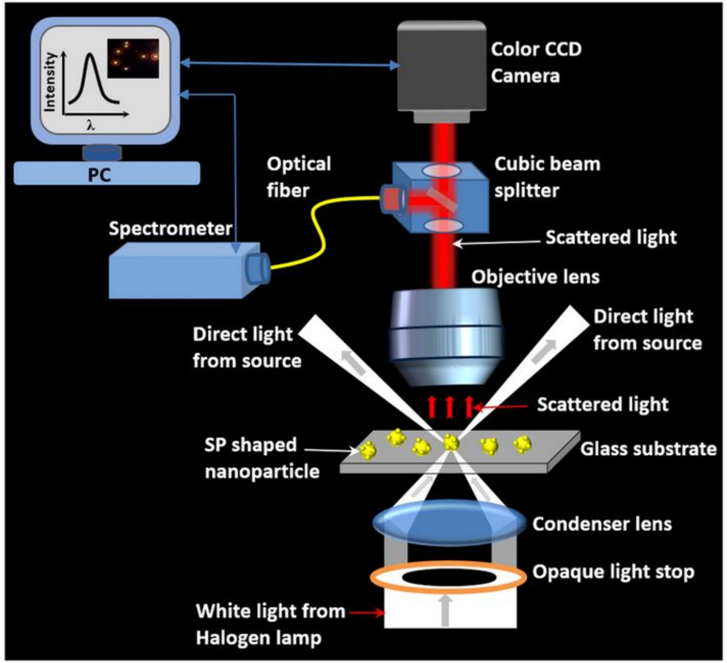


Fig 6: Illustration of a dark field microscopy setup used for capturing the scattering images and spectra of single SP-shaped Au-Ag bimetallic nanoparticles [Sibanisankar Sahoo et al. (2023)]

Wavelength-Dependent Light Scattering
5. Partial Wave Spectroscopy (PWS)

- Advanced optical diagnostic technique that analyzes spectral fluctuations in backscattered light
- Nanoscale Sensitivity
- Field Carcinogenesis Link
- Promise in identifying malignant potential in histologically normal tissues

Angle-Resolved Light Scattering

- Technique that measures the intensity of scattered light at various angles to assess morphological variations in cells and tissues.
- Sensitive to changes in scatterer properties
- Parameters that can be assessed: nuclear-to-cytoplasmic ratio, chromatin structure
- Early Detection of Carcinogenesis, Subcellular Morphology Assessment

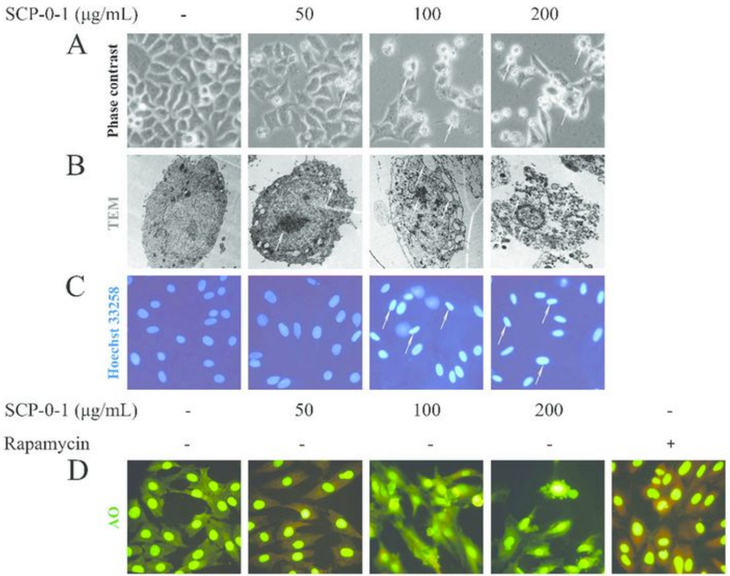
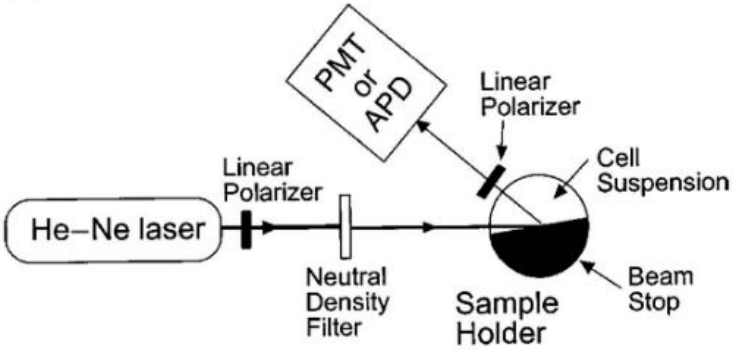


Fig 7: Morphological changes in human hepatocellular liver carcinoma (HepG2) cells after S. Chinensis polysaccharide-0-1 (SCP-0-1) treatment. [Yongling Chen et al. (2018)]

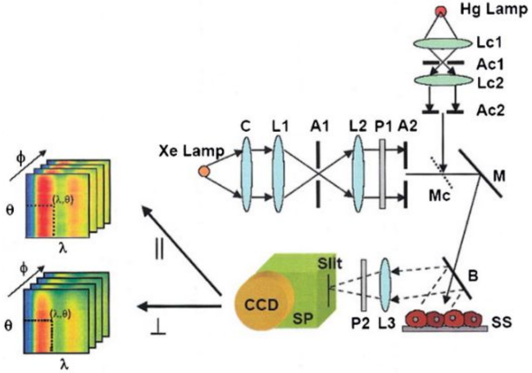
Angle-Resolved Light Scattering

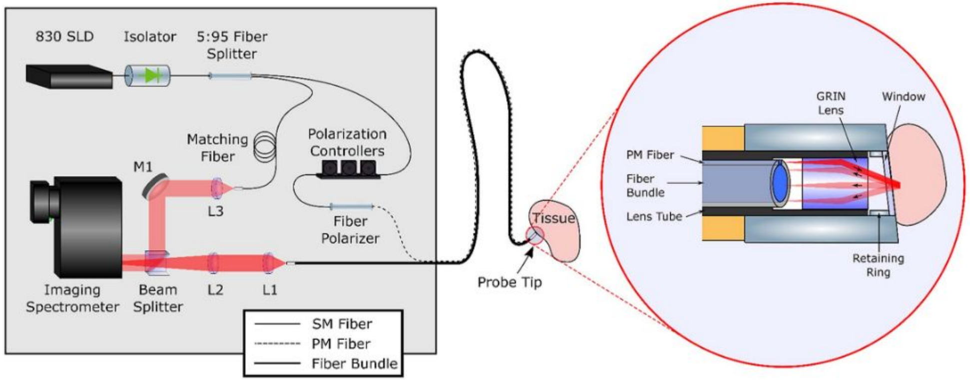
1. **Goniometric Measurements**
   a. Early investigations utilized goniometer systems to assess light scattering from: Suspended cells, isolated nuclei, mitochondria
   b. Methodology: A focused beam of light interacts with the sample, while a rotating detector captures scattered light intensity across various angles.

2. **Finite-Difference Time-Domain (FDTD) Methods**
   a. Model scattering distributions for cells with complex geometries
   b. Sensitive to differences between healthy and precancerous cells



Angle-Resolved Light Scattering





3. **Four-Dimensional Elastic Light-Scattering Fingerprinting (4D-ELF)**
   a. Captures spectral, angular, azimuthal, and polarization aspects of light scattering
   b. Aids in analyzing tissue architecture during cancer progression

4. **Angle-Resolved Low-Coherence Interferometry (a/LCI)**
   c. Combines angle-resolved backscattering with low-coherence interferometry
   d. Demonstrates high sensitivity and specificity for diagnosing dysplasia in various tissues

Fourier-Domain Methods

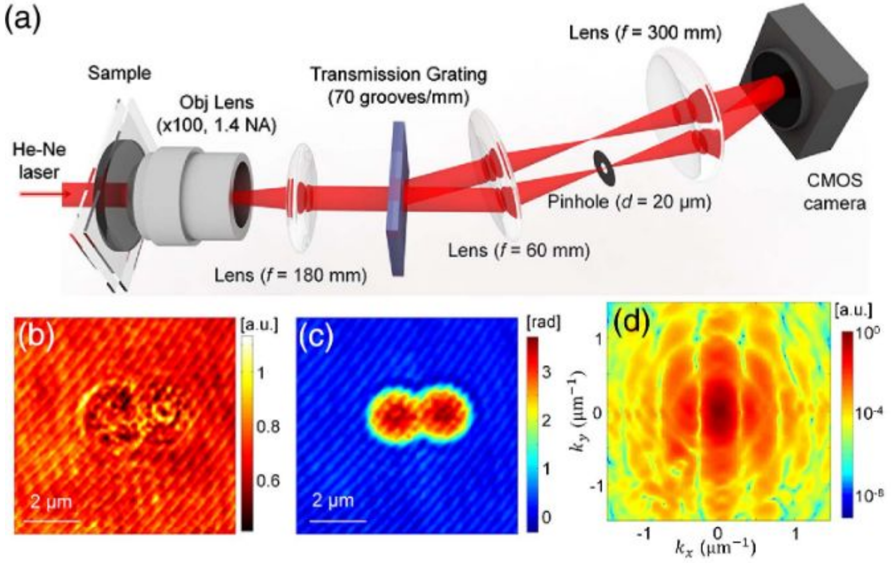
1. **Fourier Transform Light Scattering (FTLS)**

   a. Utilizes diffraction phase microscopy (DPM) to capture wavefront images near the microscope's image plane

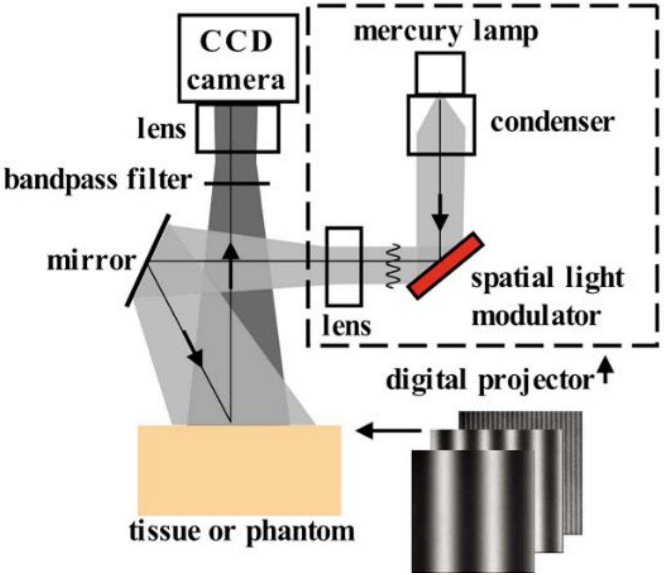
   b. High spatial resolution and capability to analyze a small number of cells

   c. It allows for the alignment and summation of scattering signals from non-isotropic cells

   d. *Applications*:
      i. Characterization of rod-shaped bacteria
      ii. Dynamic scattering analysis in neural cell cultures



Fourier-Domain Methods



2. **Spatial Frequency-Domain Imaging (SFDI)**

   a. Encodes frequency-domain information into the illumination

   b. Projects sinusoidal stripes onto a sample; analyzes scattered light to reveal depth-dependent scattering properties

   c. *Applications*:
      i. Used in dermatology for assessing burn severity and identifying skin cancer risks
      ii. Imaging brain tissue and detecting differences in disease states

Conclusions

- Techniques discussed include elastic scattering, light-scattering spectroscopy, and Fourier-domain methods.
- A common framework involves developing mathematical models to analyze tissue scattering.
- Limitations exist due to assumptions in models regarding tissue properties and variability.
- Machine learning presents a promising approach to enhance model fitting and diagnostic accuracy.
- There is a need for more fundamental research on the optical properties of biological specimens.
- Regulatory challenges can hinder the commercialization of new optical technologies.
- Continued advancements in scattering-based diagnostics rely on basic research and regulatory reform.
- Integration of supplementary techniques can improve validation of new diagnostic devices.

THANK YOU FOR THE ATTENTION