Smartphone-based Point of Care Diagnostic Testing

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1.1: Replacing Centralized Clinical Laboratories
1.2: Lateral Flow Immunochromatographic Assay

**Lateral Flow Immunochromatographic Device**

- Absorbing pad
- Control line
- Capture/test line
- Nitrocellulose membrane
- Gold conjugate pad
- Sample pad

Add sample

Gold nanoparticles with analyte specific antibodies

Capture antibody will bind gold nanoparticle-Ab-analyte complex that will appear as red line. No analyte no red line.
1.3: Rayleigh vs. Mie Scatter

Rayleigh scattering is characterized by a linear decrease in light intensity with longer wavelength ($\lambda$). The scattering is more significant with shorter wavelengths ($\lambda$), leading to the sky appearing blue.

Mie scattering, on the other hand, is more robust and remains relatively constant over the entire wavelength range ($\lambda$). It is influenced more by the size of the particles ($d$), resulting in a white appearance for clouds.

The diagrams illustrate the comparison between Rayleigh and Mie scattering, emphasizing the dependency on wavelength ($\lambda$) and particle size ($d$) for different scattering phenomena.
Fluorescence may enable us to detect the signal only, not the reflection and other noises, but it is essentially inelastic light scattering and about several orders of magnitude weaker than elastic light scattering.
2.1: Benchtop Detection System
2.2: Optimizing Mie Scattering Characteristics

TSH LFA UV Absorption for Incident Angle vs. Angle of Detection

- UV Absorption of + Ctrl / - Ctrl (l / Io)
- Angle of LFA from Irradiation Fiber
- Angle of Detection Fiber from Irradiation Fiber

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2.3: Benchtop Detection System

The graph shows the intensity (I/I₀) against the mIU/mL concentration for different conditions:
- Hypothyroid
- Hyperthyroid
- Limit of Detection

The graph indicates a clear decrease in intensity as the concentration of mIU/mL decreases, with distinct markers for each condition.
3.1: Components

- Collimating Lens
- Optical Fiber
- Lateral Flow Assay
- Assay Cover
- Main Body
- iPhone
3.2: Prototype v2.2
3.3: Prototype v2.2
3.4: External LED vs. Internal Optical Fiber
4.1: Handheld Sensitivity Results

Handheld TSH Device

Intensity (8-bit)

[TSH] (mIU/L)

- Hypothyroid
- Hyperthyroid

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4.2: Algorithm
5.1: Protocol

2. Open contents. Place cassette on flat surface.
3. Use included disposable pipette and add sample. Let stand for 90 seconds.
4. Fully insert the cassette as shown, ensuring correct orientation.
5. Add 4 large drops of TSH Diluent. Device will automatically begin timing.
6. After approximately 10 mins, results are displayed.
5.2: Applications

- **Infectious Disease**
  - Chlamydiae trachomatis
  - Toxin A (C.difficile)
  - Toxin B (C.difficile)
  - Streptococcus A/B
  - Helicobacter pylori
  - Mononucleosis
  - Tuberculosis
  - Syphilis
  - Malaria
  - Chagas
  - Lyme
  - Tetanus
  - Hepatitis B
  - Adenovirus
  - Rotavirus
  - Influenza A/B
  - Toxoplasmosis

- **Hormones**
  - TSH (Thyroid)
  - HCG (Pregnancy)
  - LH (Ovulation)
  - FSH (Menopause)
  - Prolactin (Infertility)
  - Microalbumin (Kidney/Cardiovascular)
  - PSA (Prostate)

- **Other Applications**
  - Cardiac markers: troponin i, CPK mb
  - Tumor markers: CEA, alpha fetoprotein
  - Drug screening: opiates, amphetamines, benzodiazepines, THC, barbiturates
6.1: Regulatory Affairs - Statutory Requirements

Class 2 in vitro diagnostic device
• Establishment registration, and Medical Device listing (21 CFR Part 807)
  • Quality System (QS) regulation (21 CFR Part 820);
  • Labeling requirements (21 CFR Part 801);
  • Medical Device Reporting (21 CFR Part 803);
  • Premarket notification (21 CFR Part 807);
  • Reporting Corrections and Removals (21 CFR Part 806)

510(k) approval route
• http://books.nap.edu/openbook.php?record_id=12960

Mobile Medical App regulations
• http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm263280.htm
• The app and immunoassay reader are medical devices. The iPhone is not a medical device.
6.2: Regulatory Affairs - Design Considerations

- Verification of performance specifications
- Establishment of performance specifications
- Procedure Manual
- Analyte specific validation
- Calibration and calibration verification
- Reportable range for test results using the test system
- Test system instructions and operator manuals
- Test Systems, Equipment, Instruments, Reagents, Materials, and Supplies
- Maintenance and Function Checks
- Calibration and Calibration Verification Procedures
- Control Procedures