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Quantum-Enhanced Optical Monitoring of Bone Marrow–Derived and Pluripotent Stem Cells at 1 μ m Resolution Using Squeezed-Light Interferometric Microscopy

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We use this protocol and it's working

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Disclaimer

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Abstract

We report the experimental implementation of a quantum-enhanced interferometric microscopy platform for monitoring mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and bone marrow-derived stem cells (BMSCs) at $1\ \mu\text{m}$ spatial resolution. A 5.1 dB quadrature-squeezed illumination source was integrated into a phase-stabilized Mach-Zehnder interferometer coupled with high-NA microscopy optics and sCMOS detection. The system achieves a $1.76\times$ phase sensitivity improvement beyond the shot-noise limit (SNL), corresponding to a $2.8\times$ signal-to-noise ratio enhancement in live-cell imaging. Sub-micron refractive index sensitivity (5.2×10^{-4} RIU) enabled early detection of mitochondrial remodeling and cytoskeletal disorganization in differentiating and stress-induced stem cells. These results demonstrate the translational potential of quantum-enhanced optical metrology in regenerative medicine and stem cell monitoring.

Attachments



Quantum-Enhanced

Opt...

3.9MB

Materials

Cell Sources

- Human Hematopoietic Stem Cells (HSCs): Primary HSCs were obtained from consenting donors under IRB-approved protocols and processed according to institutional guidelines.
- Cancer Cell Line: MDA-MB-231 human breast cancer cells were cultured under Biosafety Level 2 (BSL-2) conditions in compliance with institutional biosafety regulations.

Cell Culture Reagents

- Dulbecco's Modified Eagle Medium (DMEM) or appropriate HSC expansion medium
- Fetal Bovine Serum (FBS), heat-inactivated
- Penicillin-Streptomycin (100 U/mL, 100 µg/mL)
- L-glutamine (2 mM)
- Phosphate-buffered saline (PBS), sterile
- Trypsin-EDTA solution (0.05%)
- Mitochondrial membrane potential indicator (when applicable for validation experiments)

Optical and Spectroscopy System Components

- Laser Source: 1064 nm single-frequency Nd:YAG laser (linewidth <1 kHz)
- Auxiliary alignment laser (780 nm)
- Optical isolators and beam expanders
- Polarizing beam splitters and waveplates
- Periodically Poled KTiOPO₄ (PPKTP) crystal (for squeezed-light generation, if applicable)
- High-stability interferometric microscope platform
- Vibration-isolated optical table

Detection and Acquisition

- **sCMOS Camera:** Andor Zyla 4.2 PLUS
- Quantum Efficiency (QE): 82%
- Median read noise: 1.0 e⁻ rms
- Frame rate: 100 fps
- Balanced homodyne detection module (for phase-resolved measurements)
- Data acquisition workstation with high-speed frame grabber

Data Processing and Analysis

- MATLAB / Python-based signal processing environment
- Fourier-domain analysis tools for Power Spectral Density (PSD) computation
- Phase unwrapping and noise-filtering algorithms

Safety warnings



- **Laser**

and Optical Safety: Experiments involve high-intensity laser illumination (up to 100 $\mu\text{J/s}$ per sample); proper eye protection and beam containment are required.

- **Microwave**

Exposure: Quantum sensing uses 2.87 GHz microwaves; avoid direct exposure to personnel and follow institutional safety protocols.

- **Biological**

Materials: Human hematopoietic stem cells and cancer cell lines must be handled under appropriate biosafety level conditions (BSL-2).

- **Phototoxicity:**

Long-term live-cell imaging may induce phototoxic effects; maintain low exposure and verify cell viability.

- **Chemical**

Hazards: Use caution with GelMA, photoinitiators, and fluorescent dyes; handle according to MSDS guidelines.

- **Electrical**

Equipment: Ensure proper grounding and calibration of all optical and electronic instruments to prevent hazards.



Ethics statement

Stem cell testing was conducted using a quantum-enhanced interferometric spectroscopy platform operating at 1064 nm. The system enabled non-invasive, label-free characterization of cellular microstructure, mitochondrial dynamics, and early apoptotic signatures. High-sensitivity detection was achieved through low-noise sCMOS acquisition, allowing precise phase-resolved measurements under reduced photon flux conditions. This approach ensured robust quantitative assessment of stem cell viability, metabolic state, and structural integrity while preserving cellular physiology.

All experiments involving stem cells were performed in full compliance with institutional governance standards and received approval from the appropriate Institutional Review Board (IRB). Cells were obtained from consenting donors under formally approved protocols, and all procedures were conducted in alignment with the principles outlined in the Declaration of Helsinki. The MDA-MB-231 cancer cell line was handled strictly under institutional Biosafety Level 2 (BSL-2) regulations. No direct human or animal subject interventions were performed as part of this study. All experimental activities adhered to established ethical frameworks governing laboratory safety, stem cell research, and responsible conduct of research.

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