We have developed a high throughput technology to apply forces to biological systems. This Multiforce High Throughput System (MHTS) uses magnetic fields to non-invasively apply forces to magnetic particles of sizes ~0.1 - 10 µm. The MHTS can be used make mechanical measurements of cells, tissues, and polymers, and to study the transport of magnetic probes through these materials. We also report on the design of a multiscope, designed to simultaneously observe 12 wells in a 96-well microplate.

The passive and driven microbead techniques we employ are destructive and non-invasive, explore a broad range of length scales and bead-sample interactions, and probe a broad force range and bandwidth.


Multiforce High Throughput System (MHTS)

Below, a cartoon of a single magnetic force system. The blue structure represents the magnets block, which houses the drive coils, shown at right with three drive coils inserted.

Magnetic force equation:

\[ F = \frac{\pi D^3}{2 \mu_0} \mu_r - \frac{1}{\mu_r} + 2 \nabla B^2 \]

The µ-metal foil, shown in dark grey, above-left, is mounted on glass. The 16-well implementation is above-right.

Key features of MHTS Design:
- Microplate design
- High-NA optics compatible
- Independent well control
- Temperature control
- Cell culture compatible
- 20µL sample size
- 0-100 Hz Force bandwidth

Calibration, Crosstalk, and Degauss (data not shown)

The MHTS force range is 1pN – 10 nN, depending on probe size. Well-to-well crosstalk is shown to be 3% in a limiting case where all but the imaged well are maximum drive current. We have shown that a damped AC drive current can effectively remove (“degauss”) remnant magnetization due to hysteresis.

Experiments

High throughput mucus rheology

Shear thinning profile of 4% Porcine gastrin mucus measured by the MHTS. The rheology of mucus is critical to understand its function. For example, shear thinning may play a role in mucociliary clearance.

Panoptes: 12-well Optical Microscopy

We are developing a system for imaging up to 12 specimen wells at a time (cartoon at right). We are currently testing components in a single-objective configuration.

Z-focus with no moving parts. We have integrated an electronically controlled liquid lens with a 40x objective. We are aware of no other objective with built-in focus adjustment and no moving parts.

Automatic Particle Tracking. CISMM VideoSpotTracker automatically identifies trackable particles. Particle tracking has historically been the bottleneck in these manipulation experiments.

Experiments

High throughput blood clot characterization

Fibrin gels (shown in confocal, above), are the primary structural component of a blood clot. Their structure has been correlated with heart disease risk and diabetes.

We have developed a high throughput assay for measuring fibrin clot structure. Below, the diffusion coefficients of 500 and 260 nm PEG-polystyrene particles drop as the gel around them becomes more dense. This experiment has been made possible by automatic particle tracking using Video Spot Tracker, which analyzes thousands of particle traces per clot type.

High throughput cell mechanics

Collab. with Steve Rogers, Biology

Variation in the compliance of cells with and without an inhibitor to cytoskeletal remodeling, measured by the MHTS.

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