

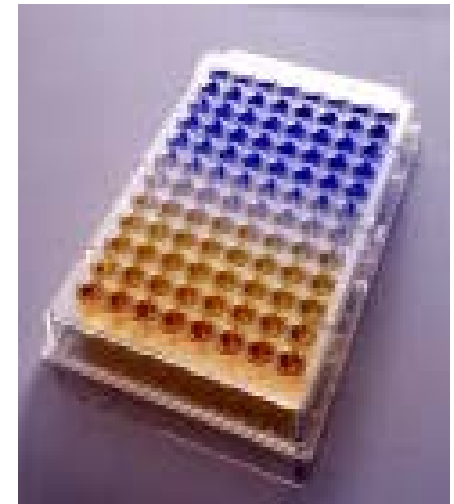
Susceptibility-Matched Multiwell Plates for High-Throughput Screening by Magnetic Resonance Imaging and Spectroscopy

Kenneth W. Fishbein, Ph.D.

Laboratory of Clinical Investigation

National Institute on Aging

National Institutes of Health



Technology

- ❖ **High-throughput screening by NMR spectroscopy offers:**
 - ❖ Non-destructive, detailed analysis of chemical composition and structure
 - ❖ Samples may be pure chemicals or mixtures
 - ❖ Opaque or dirty samples can be analyzed
- ❖ **Nuclear magnetic resonance (NMR) spectroscopy** has many applications in clinical chemistry, drug discovery and pharmaceutical quality control *but*:
 - ❖ Samples must be transferred to special tubes or flow cells
 - ❖ Samples are scanned one at a time

This increases risk of contamination and sample loss and limits potential throughput.

- ❖ **NMR-compatible multiwell plates ?**
 - ❖ Would eliminate need for sample transfer
 - ❖ Could scan 96 wells in parallel
 - ❖ Could be handled by standard lab robots for additional assays

Technology

❖ Susceptibility-matched multiwell plates permit NMR analysis of samples without transferring them to tubes or flow cells

- ❖ Sample throughput is increased
- ❖ Sample loss and contamination are avoided
- ❖ Sample handling is minimized, enhancing safety



Standard 96-well
polystyrene plate



Solid polyetherimide
(ULTEM) plate for
aqueous samples

❖ Prototype plates built and demonstrated.

- ❖ U.S. Patent Application 12/083,501 filed 6/25/2009

MR Detection of Nanoparticle Probes by Högemann et al.

119 *Bioconjugate Chem.*, Vol. 13, No. 1, 2002

Högemann et al.

MR imaging

Signal intensity

T2 map

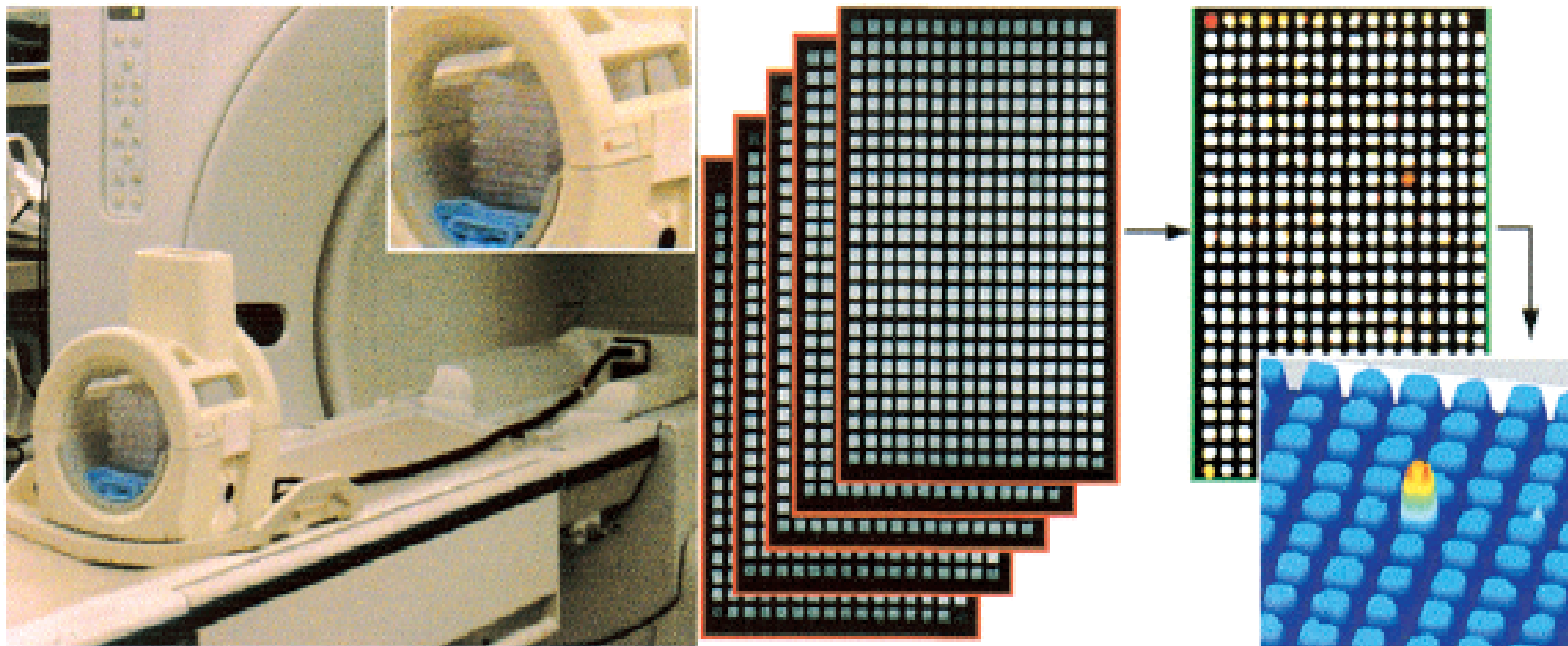


Figure 1. Use of a MR imager for high throughput screening. Microtiter plates were imaged in a quadrature coil with different pulse sequences (variable TE) to yield a series of images for each plate. Signal intensity data were processed to yield a T2 map indicating wells with "hits".

Commercial Applications

⊕ **NMR spectroscopy is already used for:**

- ⊞ Detailed analysis of blood lipids (NMR LipoProfile®)
- ⊞ Evaluation of drug-target interactions
- ⊞ Detection of contaminants in food, industrial chemicals and drugs

⊕ **NMR-compatible multiwell plates would:**

- ⊞ Reduce sample handling needed prior to NMR
- ⊞ Minimize loss of valuable samples during analysis
- ⊞ Minimize contamination of samples or apparatus
- ⊞ Increase sample throughput

⊕ **NMR-compatible multiwell plates have potential applications for high-throughput screening of:**

- ⊞ Blood serum and other body fluids
- ⊞ Potential drugs and drug-target complexes
- ⊞ QC for pharmaceutical and chemical products

Collaboration Opportunities

- ✦ Collaborators are sought for product development:
 - ❖ *Numerical simulation and optimization of plate design*
 - ❖ *Realistic test samples to demonstrate practical applications*
 - ❖ *Development of dedicated NMR coils for improved sensitivity*
 - ❖ *Design of apparatus for true parallel scanning (e.g., multi-channel coils)*
 - ❖ *Development of practical manufacturing techniques*
 - ❖ *Demonstration of compatibility with existing lab robots*
 - ❖ *Side-by-side comparison with NMR sample changers and flow probes*
 - ❖ *Extension to magnetic nanoparticle-based immunoassays*



Contact Information

✚ For further information contact:

✚ Licensing:

Michael Shmilovich

(301) 435-5019

shmilovm@mail.nih.gov

✚ Collaboration:

Nicole Darack Guyton, Ph.D.

(301) 435-3101

darackn@mail.nih.gov