AI Meets Quantum Mechanics:
Unravelling the Molecular Fingerprints of Brain Function and Diseases

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Complexity of the Brain

**FUNCTION**
- Disease
- System Coordination
- Pathways
- Activation
- Cellular Communication
- Molecules
- Genomics

**STRUCTURE**
- Body
- Organ
- Tissue
- Cell-Cell/ECM
- Cells
- Protein Interactions, Metabolites
- Proteins
- mRNA
- DNA

Biological & Physiological Networks in Disease
Brain Mapping: Global Efforts

The Decade Of The Brain
1990 - 2000

Connectome:
A map of neural connections in the brain

HUMAN BRAIN PROJECT

The BRAIN Initiative

China Brain Project
- **Stern–Gerlach experiment (1922)**

- **Relativistic Schrödinger equation (Paul Dirac, 1928):**
  \[
  i\hbar \frac{\partial \psi}{\partial t} = -\frac{\hbar^2}{2m} \nabla^2 \psi + V\psi \rightarrow i\hbar \frac{\partial \psi}{\partial t} = H\psi
  \]

- “There is nothing nuclear spins will not do for you as long as you treat them as human beings”, Erwin Hahn

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- **Spectroscopy**

- **Imaging**
Conventional MRI

Data Acquisition:

\[ s(k, t) = \int \int \rho(x, f) E(x, f; k, t) dx df \]

Image Reconstruction:

Fourier encodings at the Nyquist rate

Fourier representation of image functions

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Data Acquisition:

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Image Reconstruction:

Fourier encodings at the Nyquist rate

Fourier representation of image functions
$\rho(x, f) = \sum_{m=1}^{M} \sum_{l=1}^{L} c_{ml}(x) \phi_{ml}(f)$

$\psi(x, t) = \sum_{l=1}^{L} c_l(t) e^{-\frac{iE_l}{\hbar} t} \phi_l(x)$

Quantum Mechanics Simulation

AI-Powered MRI

Training Data
“SPICY” AI-Powered MRI

Water

B₀, B₁⁺, B₁⁻

T₁, T₂, PD, T₂*, MWF, QSM

NAA, Cr, Cho, mln, Glu, Gln, GABA, Lac
Metabolic Imaging of Brain Tumor

**Glucose**

- Glucose → Glucose-6-P
- ADP + NAD+ → ATP + NADH

**Pyruvate**

- Glucose-6-P → Pyruvate
- Pyruvate → Lactate

**Glycolysis**

- Lactate Production
- Lactate → Oxidative Phosphorylation

**Oxidative Phosphorylation**

- Acetyl-CoA → TCA Cycle
  - CO₂ + NAD⁺ + H⁺ → Glx
  - NADH + H⁺ → NAD⁺
  - ATP

**Electron Transport Chain**

- Complexes I-V
- ATP
- ADP + P → ATP

**Aerobic Glycolysis**

- Lactate → ATP
- ATP

**MPRAGE**

- Lac
- Cho/NAA
Differentiation of Different Tumors

1. T\textsubscript{1c}, T\textsubscript{2w}, NAA, Cho, Lac, Gln

2. T\textsubscript{1c}, T\textsubscript{2w}, NAA, Cho, Lac, Gln
Imaging Ischemia Stroke: Penumbra Characterization

Acquisition Time: 8 minutes
Spatial Resolution: 2.0 x 3.0 x 3.0 mm³

Li*, et al., Brain, Nov. 2020 (Cover Feature Article)
Imaging Ischemia Stroke: Onset Time Prediction

Lin, et al., JMRI, Sep. 2023 (Cover Feature Article)

ISMRM W. S. Moore Award, 2023
Metabolic Imaging of Multiple Sclerosis

Detection of MRI-invisible pre-lesion
Metabolic Imaging of Alzheimer’s Disease

- NAA reduction
  Neuron/synaptic dysfunction or Neuron loss
- mI elevation
  Microglia and astrocyte activation
Monitoring Treatment Response: Radiation Therapy

Scan #1: 2 weeks
Scan #2: 4 weeks
Scan #3: 3 months
Scan #4: 6 months
Monitoring Treatment Response: Transcranial Magnetic Stimulation

**Left DLPFC (Treatment)**
- **Glu:** +27.2%, p = 0.011 (Baseline: Before TMS, After TMS: After TMS)
- **GABA:** +35.1%, p = 0.039 (Baseline: Before TMS, After TMS: After TMS)

**Right DLPFC (Opposite)**
- **Glu:** ~7.1%, p = 0.457 (Baseline: Before TMS, After TMS: After TMS)
- **GABA:** ~2.1%, p = 0.816 (Baseline: Before TMS, After TMS: After TMS)

**Brain Imaging**
- **Radius: 3 mm**
  - **Glu:** +36.4% (Before: Before, After: After)
  - **GABA:** +42.9% (Before: Before, After: After)
- **Radius: 6 mm**
  - **Glu:** +27.2% (Before: Before, After: After)
  - **GABA:** +35.1% (Before: Before, After: After)
- **Radius: 9 mm**
  - **Glu:** +17.7% (Before: Before, After: After)
  - **GABA:** +24.1% (Before: Before, After: After)

**Radius: 3 mm**
- **Glu:** -0.4% (Before: Before, After: After)
- **GABA:** +8.5% (Before: Before, After: After)

**Radius: 6 mm**
- **Glu:** -7.1% (Before: Before, After: After)
- **GABA:** -2.1% (Before: Before, After: After)

**Radius: 9 mm**
- **Glu:** -3.3% (Before: Before, After: After)
- **GABA:** -0.8% (Before: Before, After: After)
Towards Unraveling Structural, Functional, Molecular Fingerprints of Brain Function and Neurodegenerative Disorders