

Towards Automatically Optimized Multi-Metabolite CEST Fingerprinting – When a Computational Graph Meets Proton Exchange

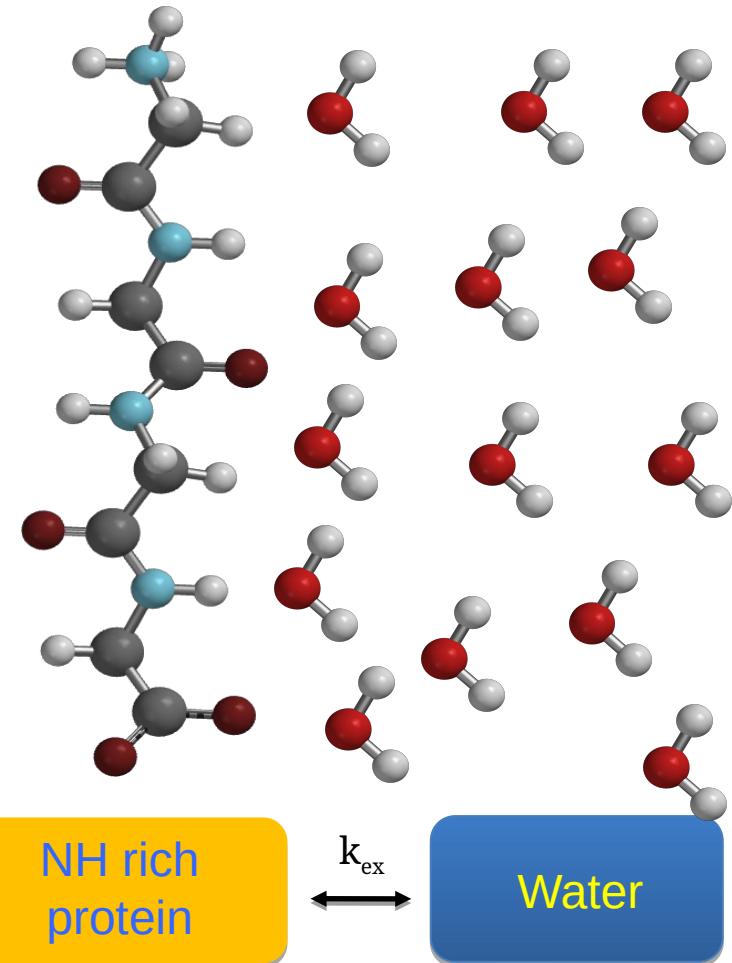
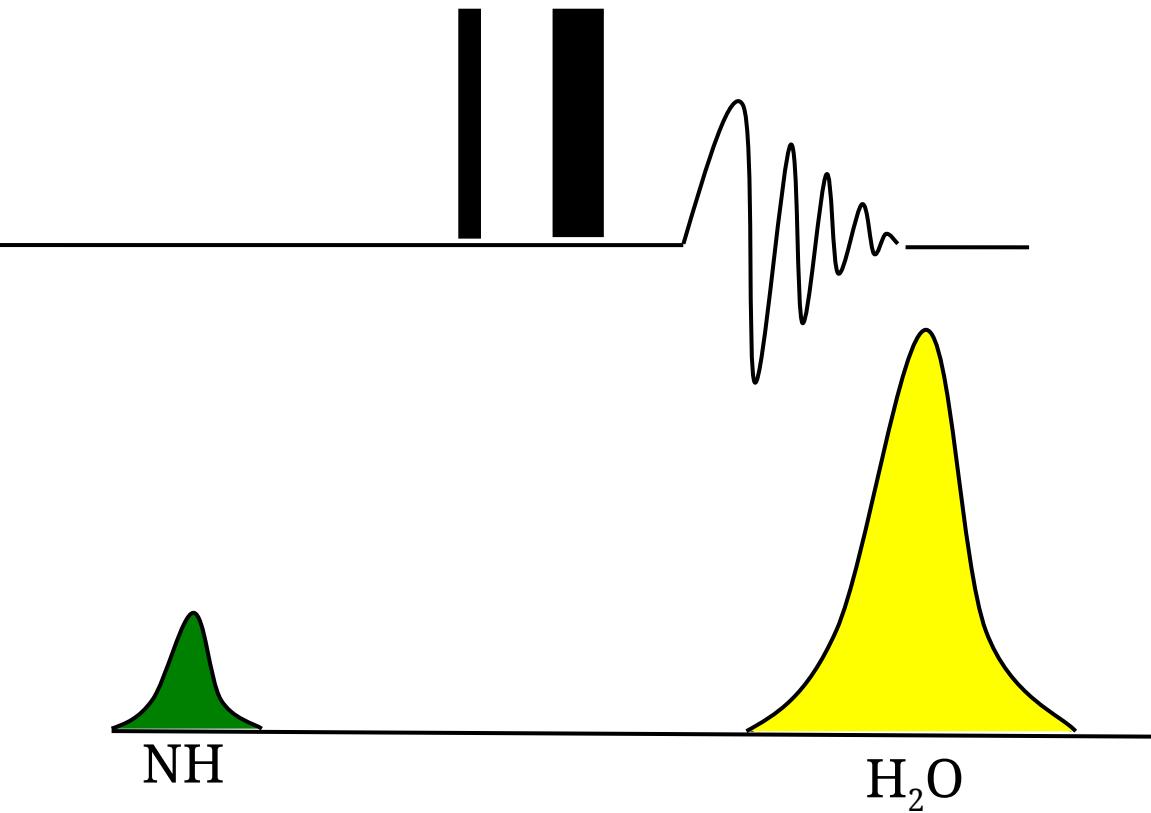
Or Perlman

School of Biomedical Engineering

Sagol School of Neuroscience

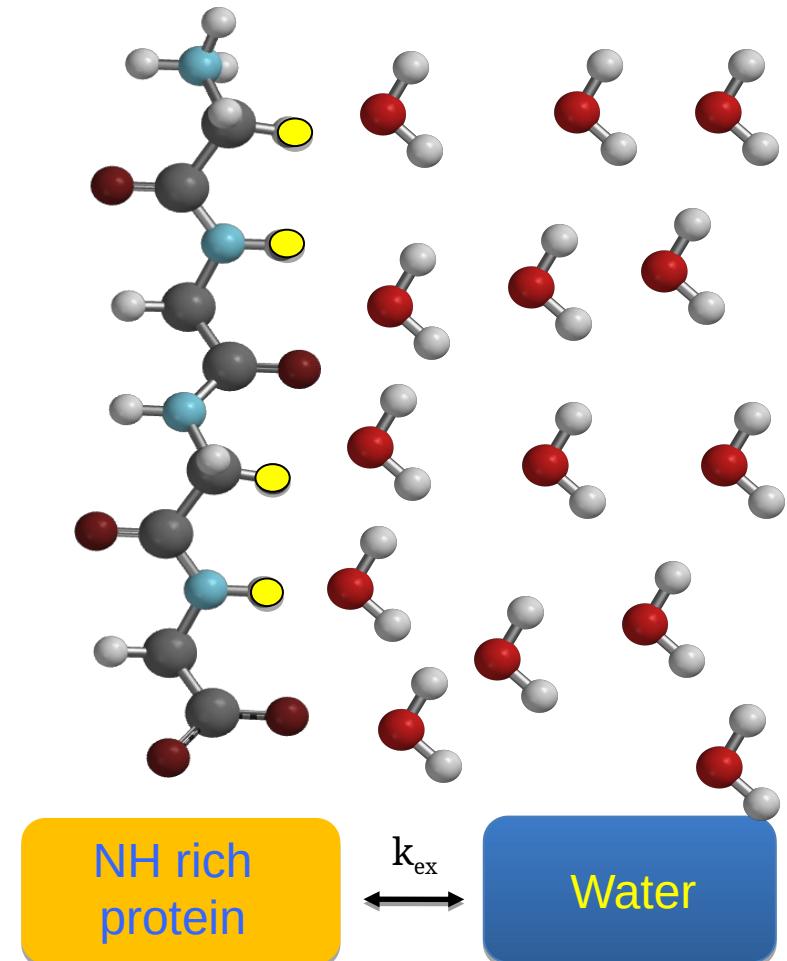
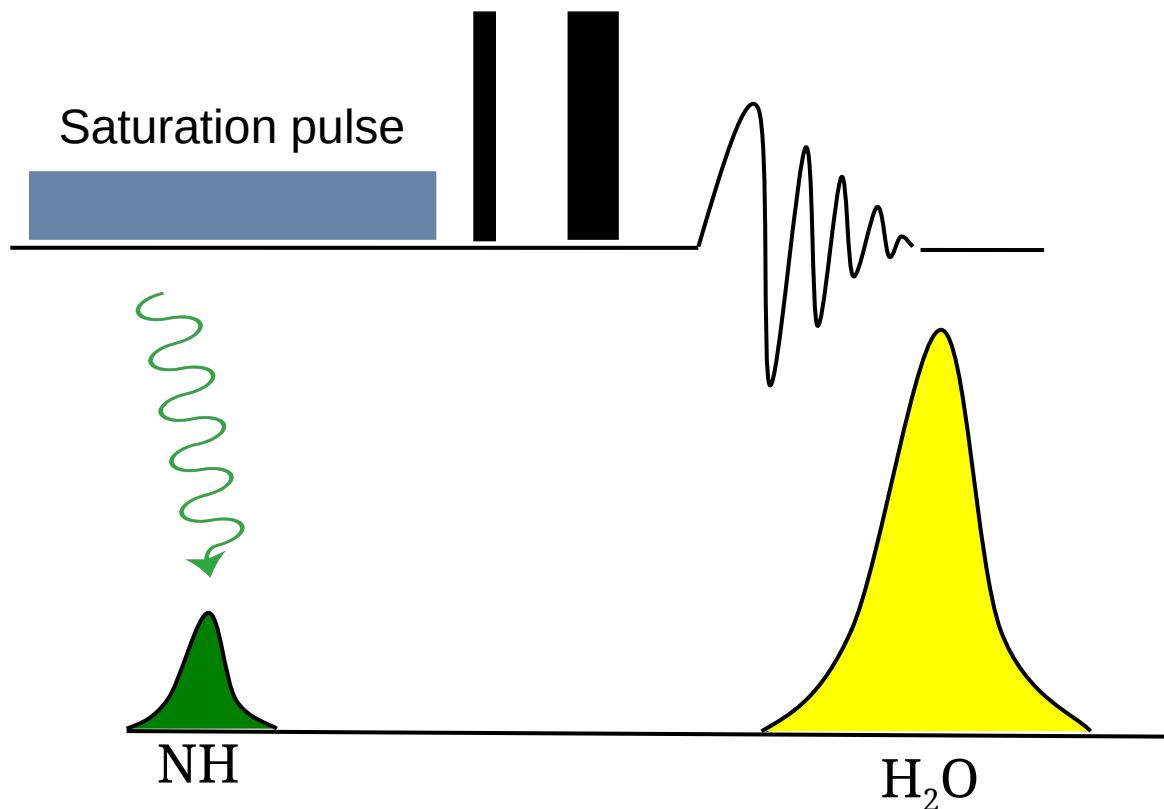
Tel Aviv University

Chemical Exchange Saturation Transfer (CEST)

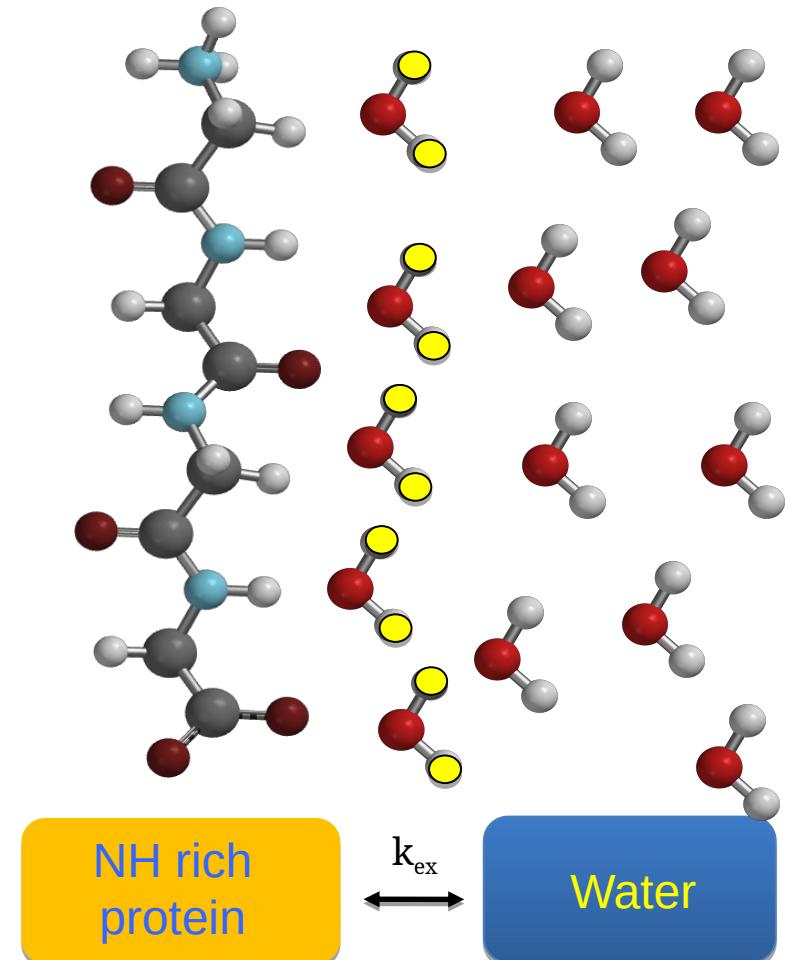
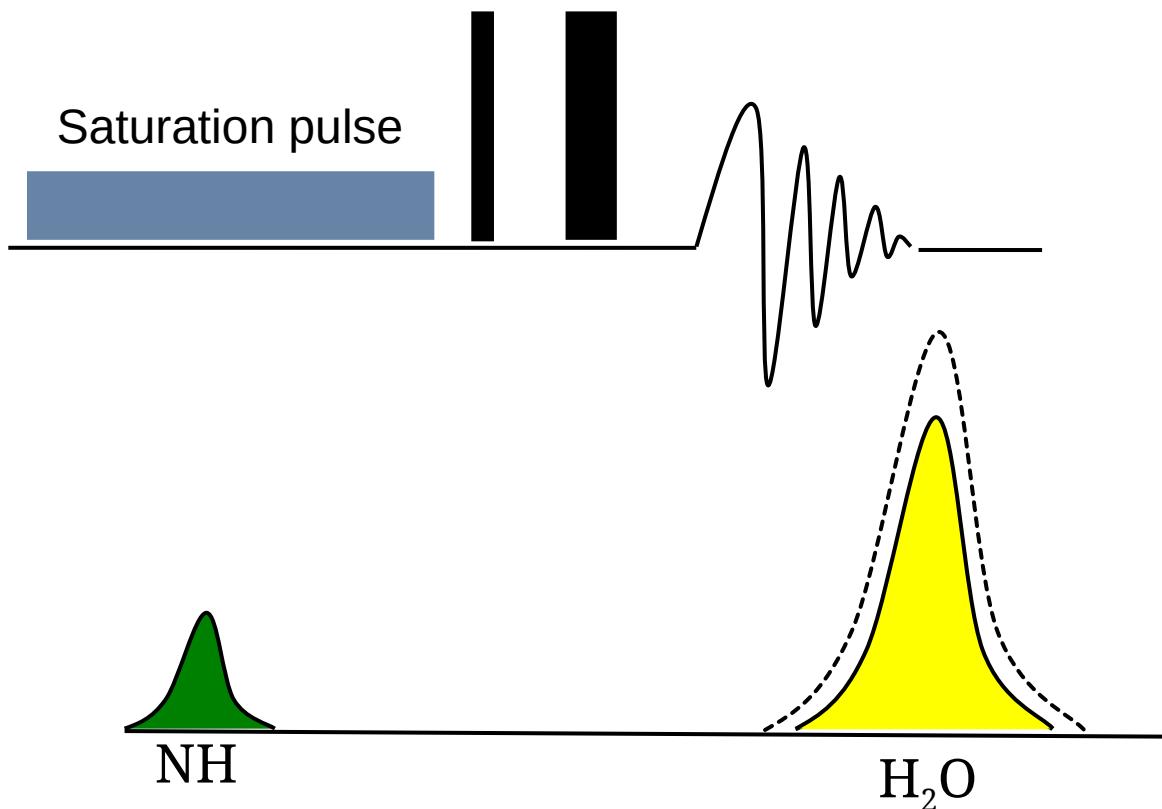


Animation courtesy of Prof. Christian Farrar

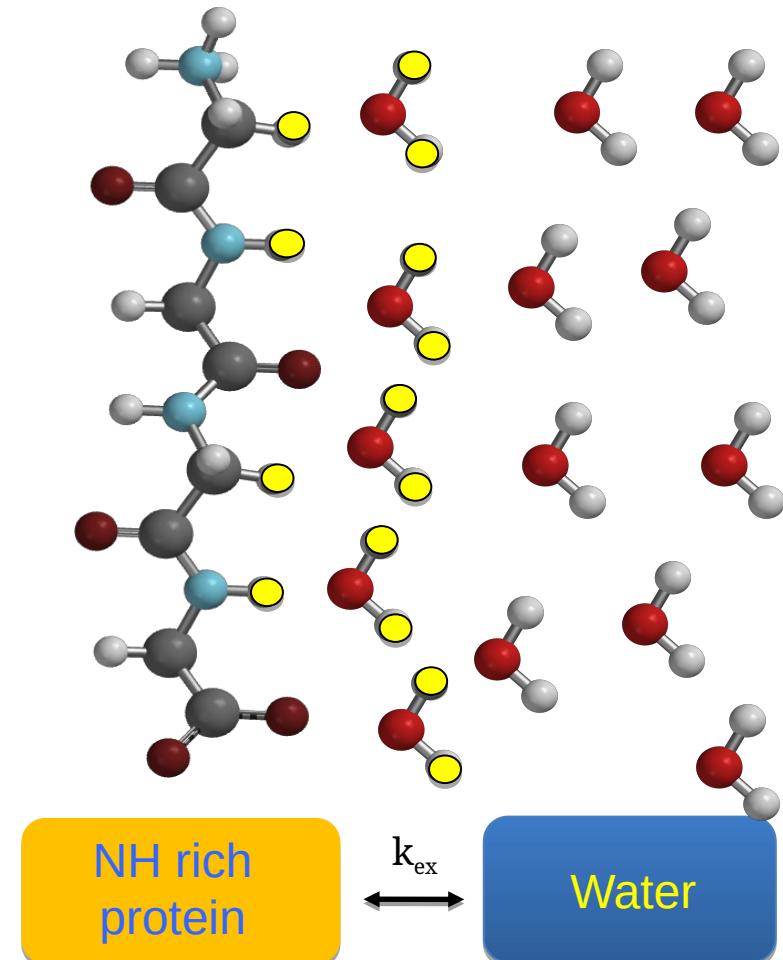
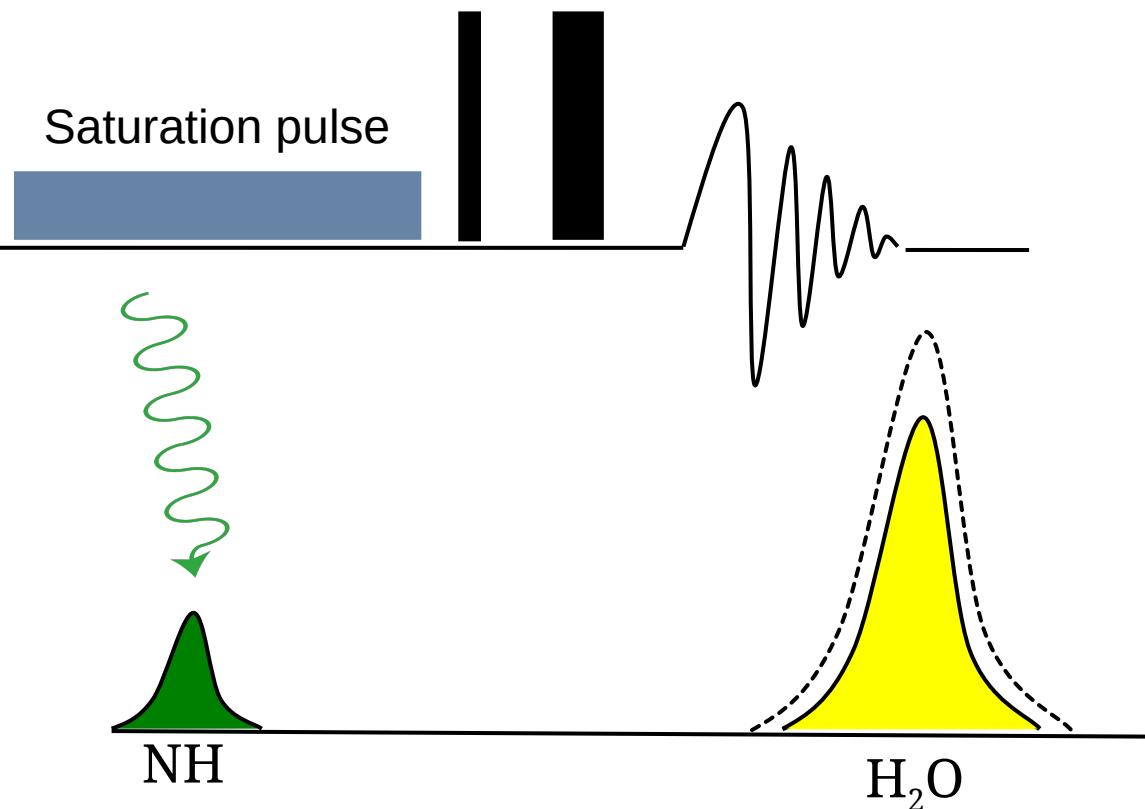
Chemical Exchange Saturation Transfer (CEST)



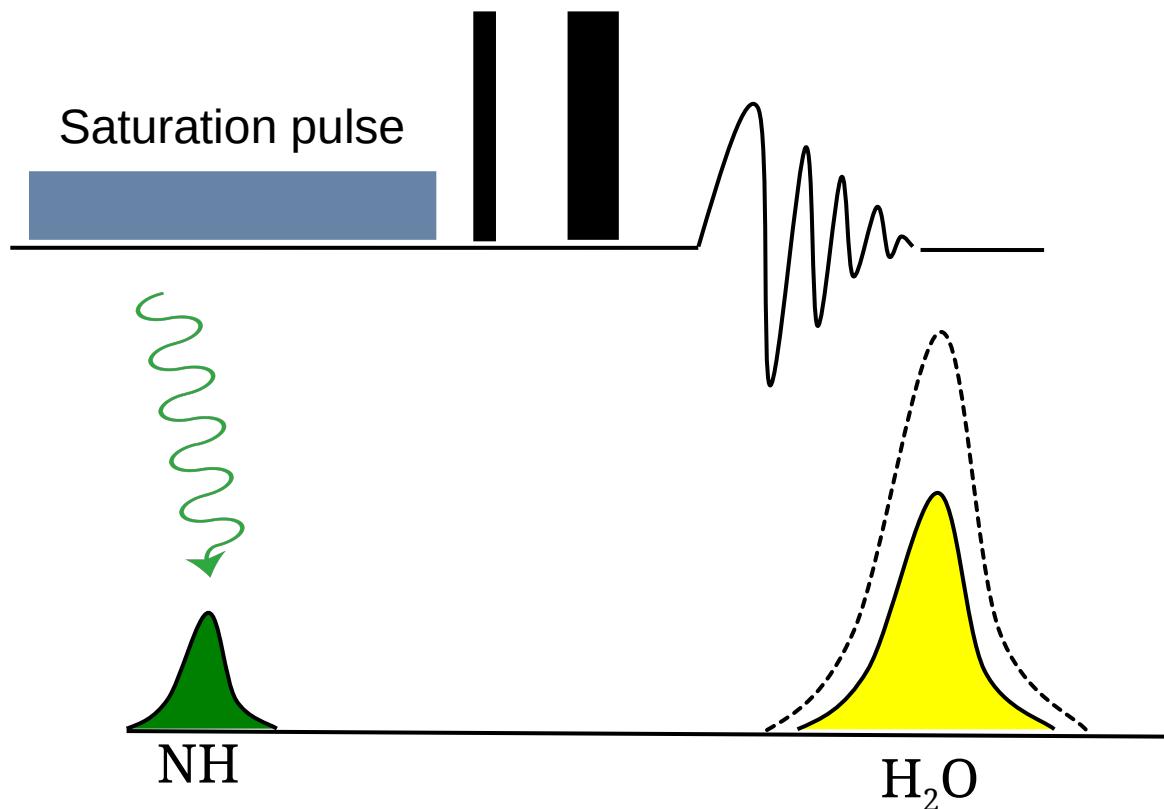
Chemical Exchange Saturation Transfer (CEST)



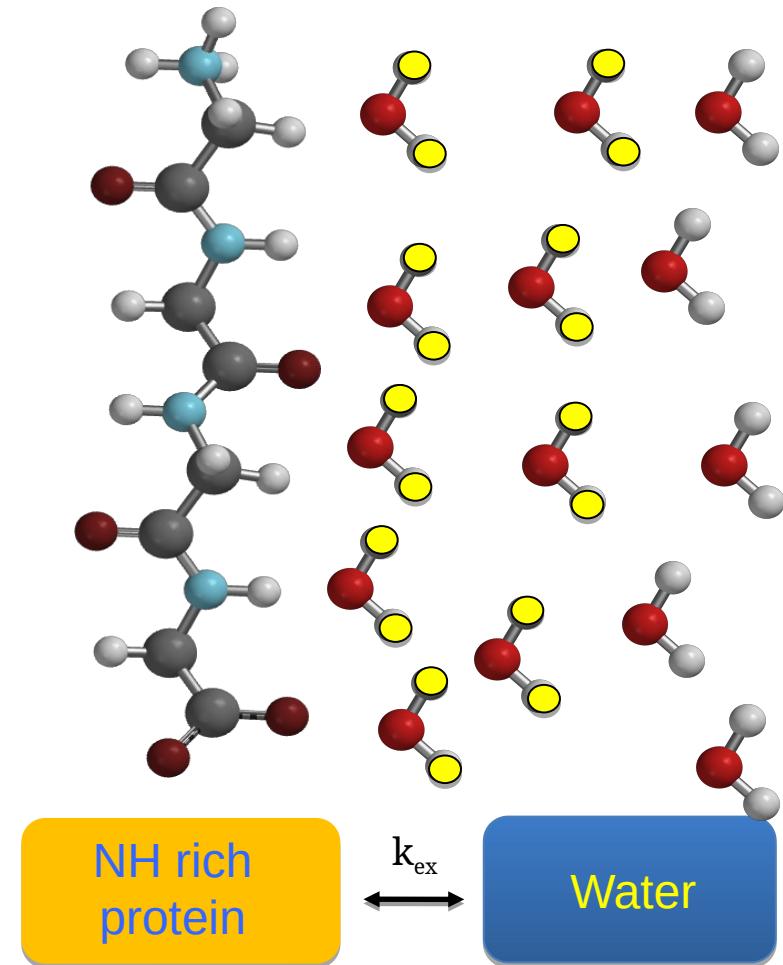
Chemical Exchange Saturation Transfer (CEST)



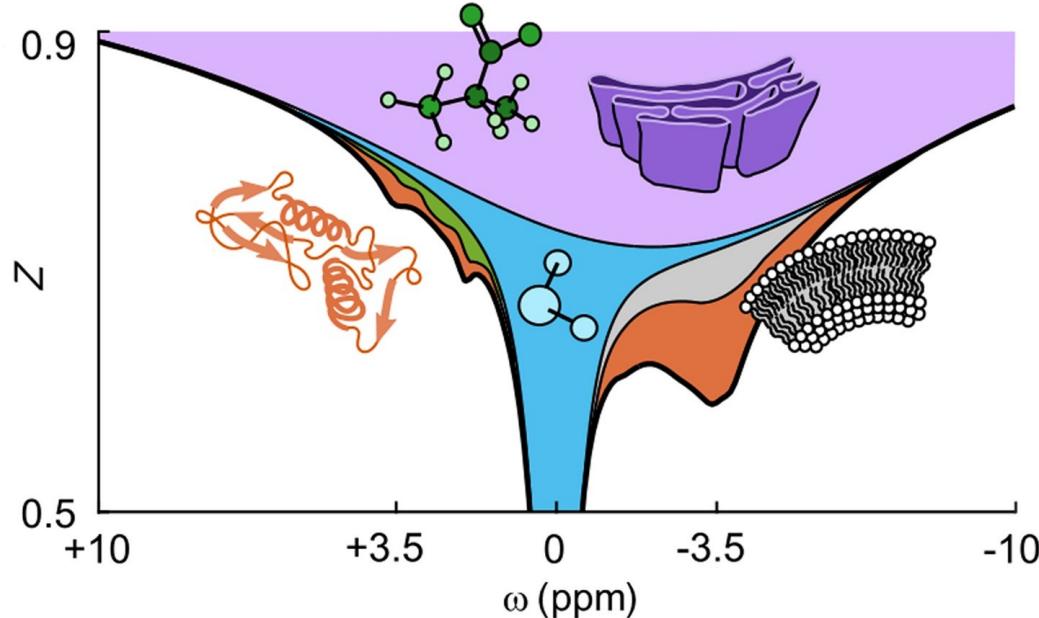
Chemical Exchange Saturation Transfer (CEST)



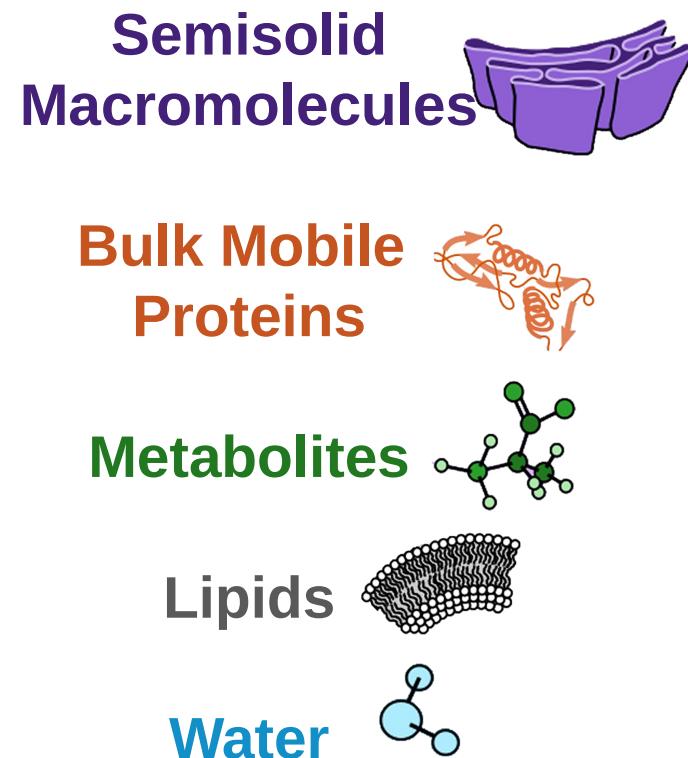
Fast exchange as saturation amplifier:
Low concentrations can be detected



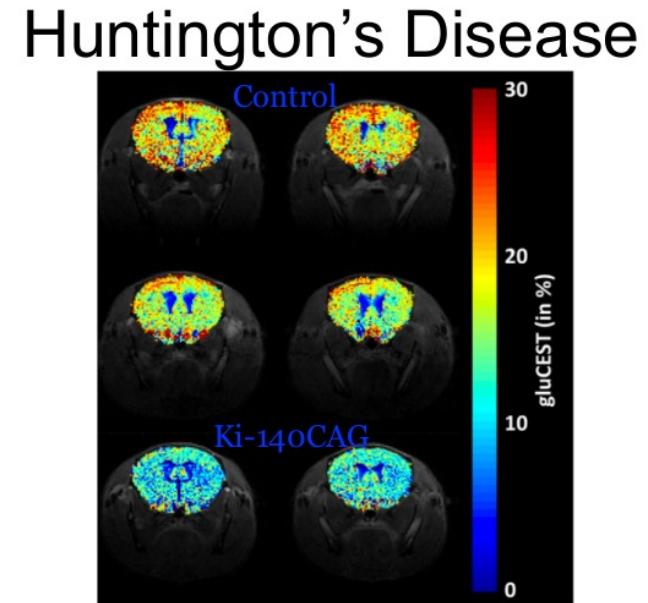
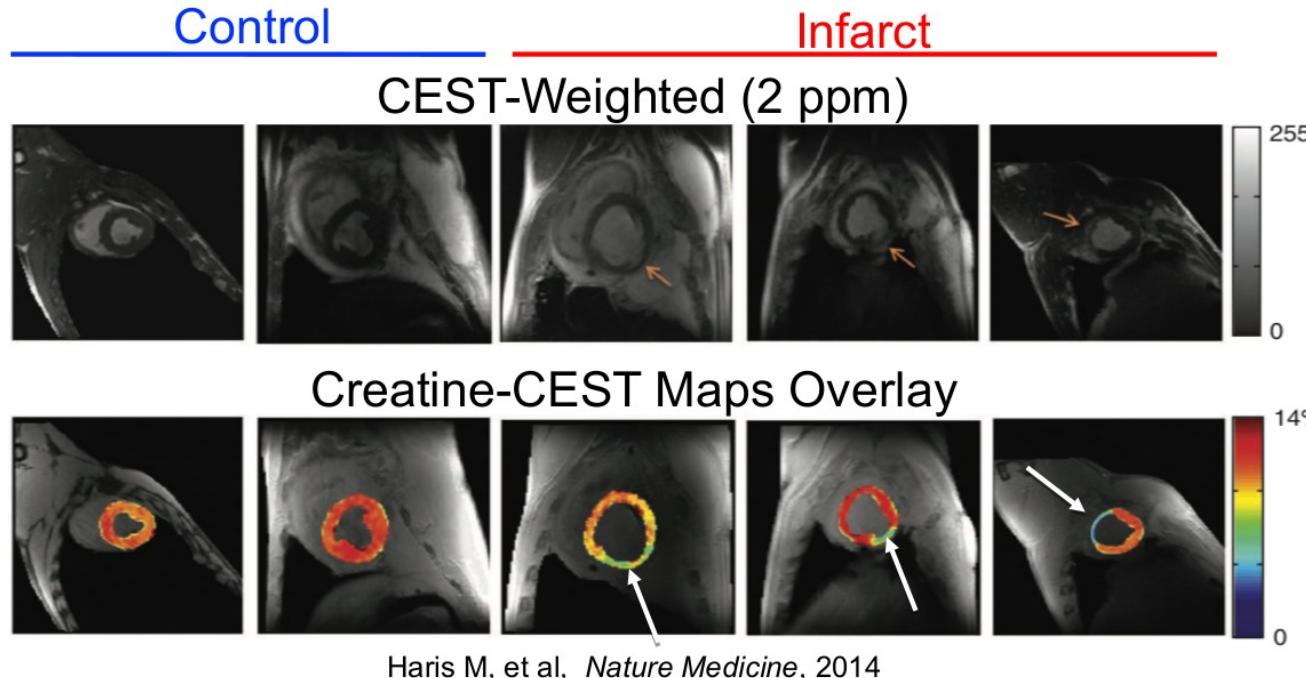
CEST MRI Contrast Mechanism



Goerke et al., *NMR Biomed.*, 2018



CEST-Weighted Imaging

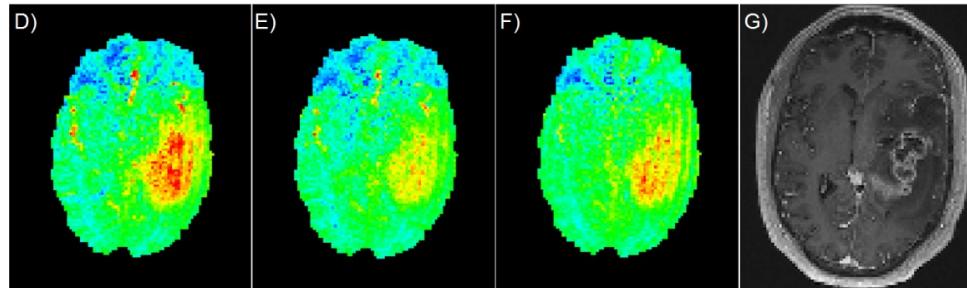


Pepin J, et al, *NeuroImage* 2016

CEST Challenges: (1) Qualitative

CEST contrast depends on:

- Volume fraction of labile protons (f_s)
- Proton chemical exchange rate (k_{sw})
- RF saturation time (t_{sat}) and power (B_1)
- RF saturation efficiency (α)
- Water relaxation rates R_1^w/R_2^w

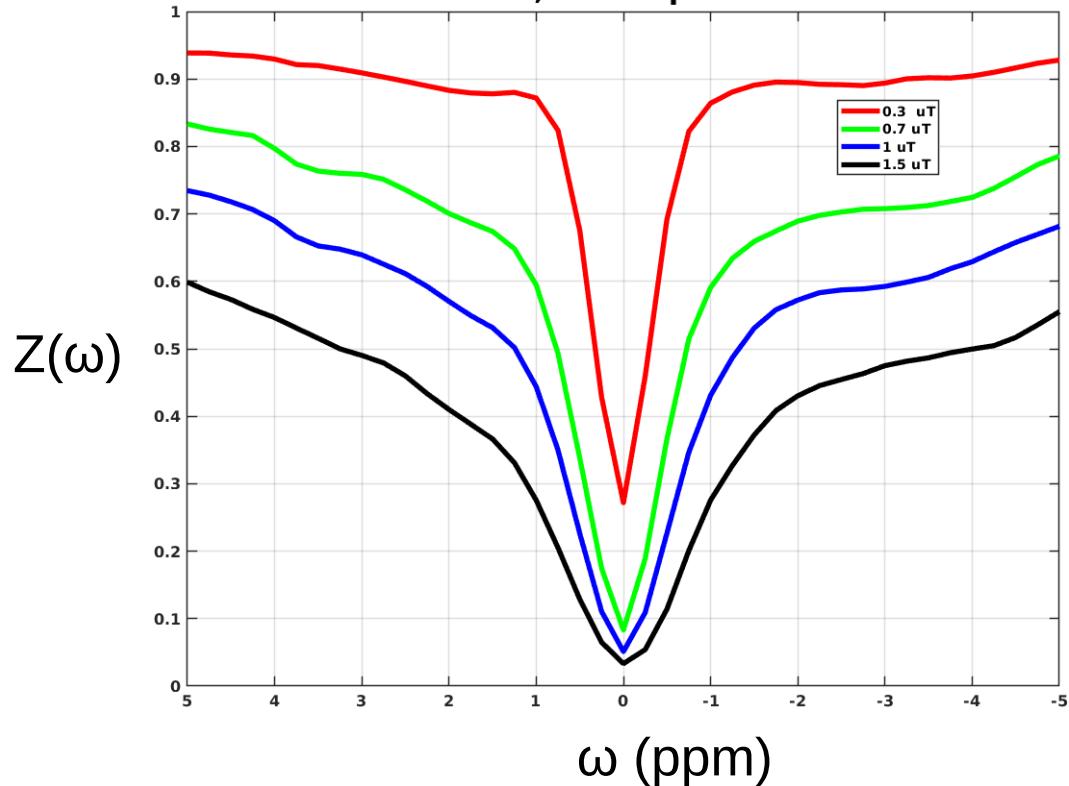


Herz et al. *Magn Reson Med.* 2021

$$\alpha = \frac{(\gamma B_1)^2}{(\gamma B_1)^2 + k_{sw}(k_{sw} + R_2^w)}$$

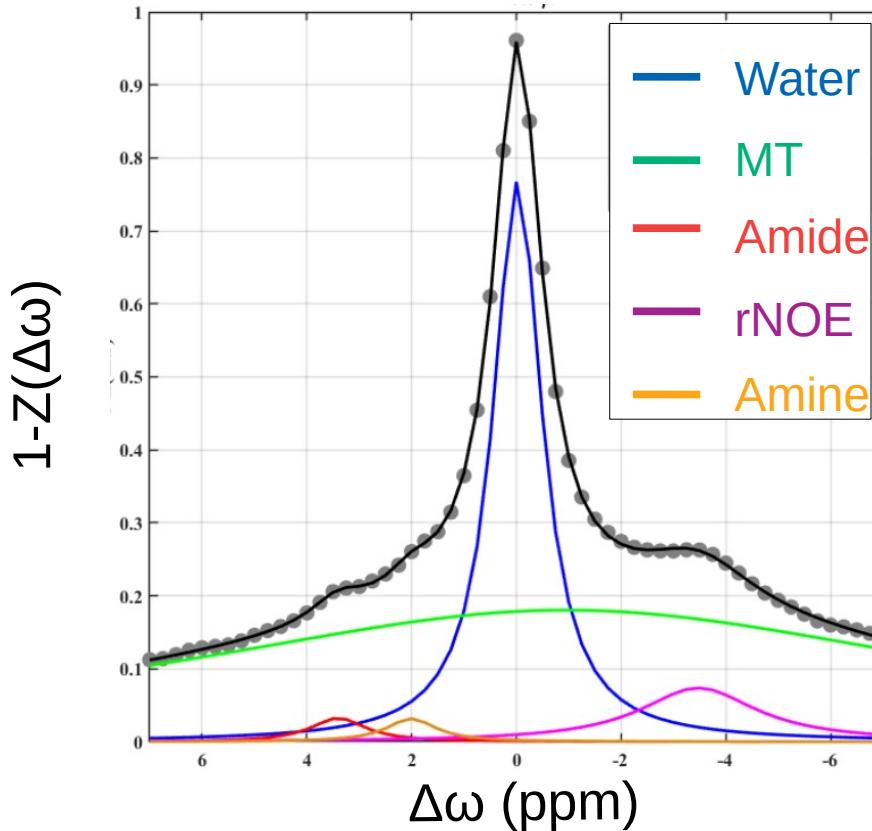
$$MTR_{asym} = \frac{\alpha \cdot f_s \cdot k_{sw}}{R_1^w + \alpha \cdot f_s \cdot k_{sw}} \left(1 - e^{-(R_1^w + \alpha \cdot f_s \cdot k_{sw}) t_{sat}} \right)$$

CEST Challenges: (2) Lengthy



Multi-B₁ Z-spectra acquisition ~ tens of minutes to > 1hr

CEST Challenges: (3) Multi-Pool Environment



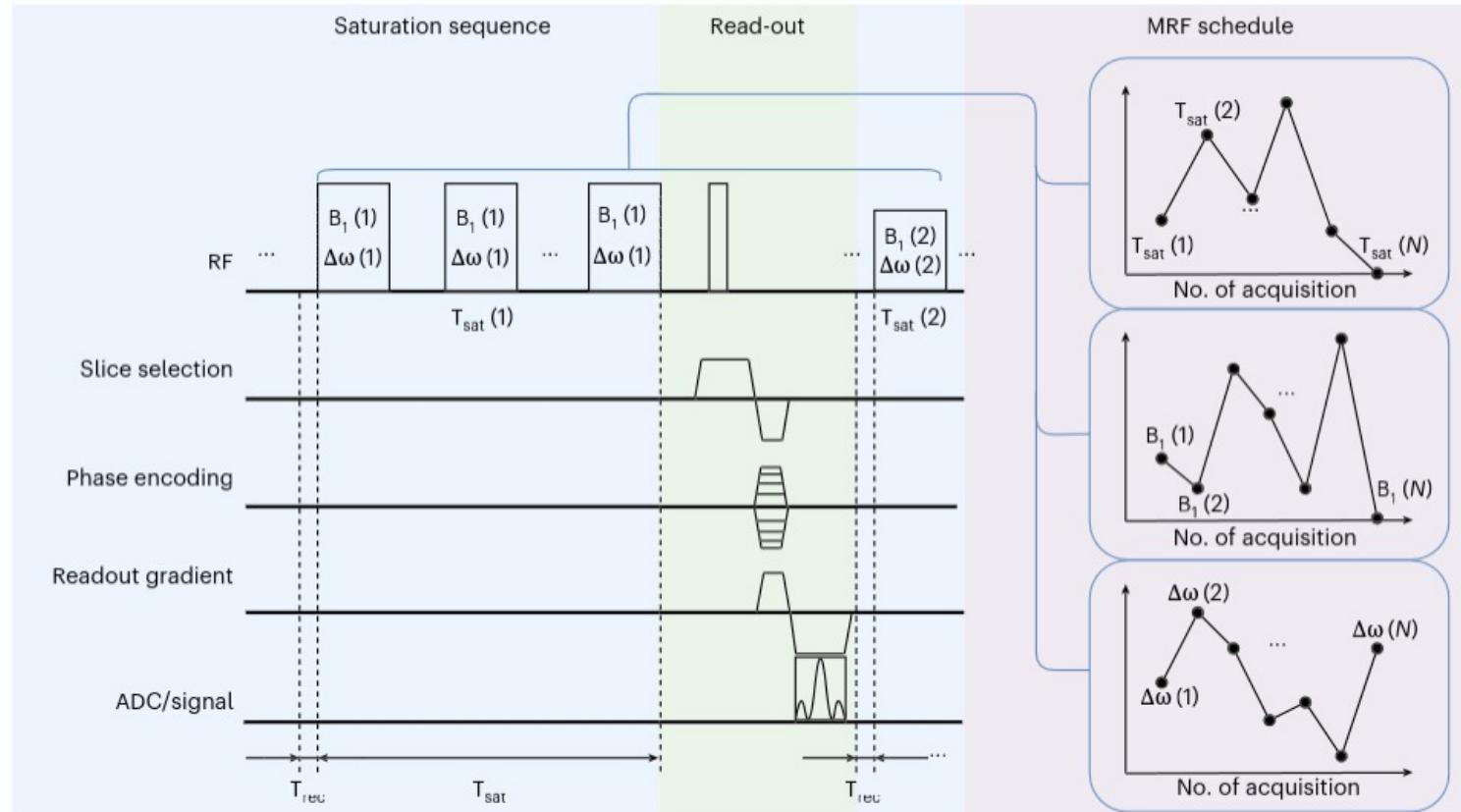
Perlman et al. *Sci. Rep.* 2020

Multiple exchangeable proton pools complicate data analysis

Desired Outcome

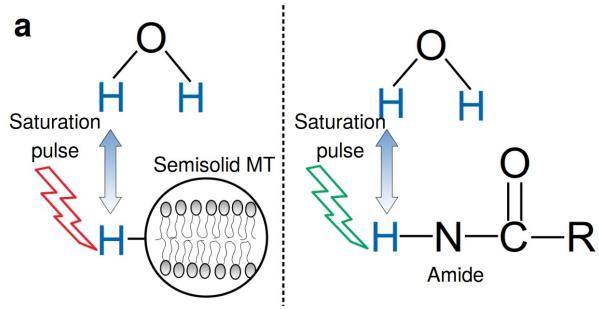
Establish a fast, specific, and quantitative
molecular CEST MRI method

CEST MRF



CEST MRF

Acquisition Schedule

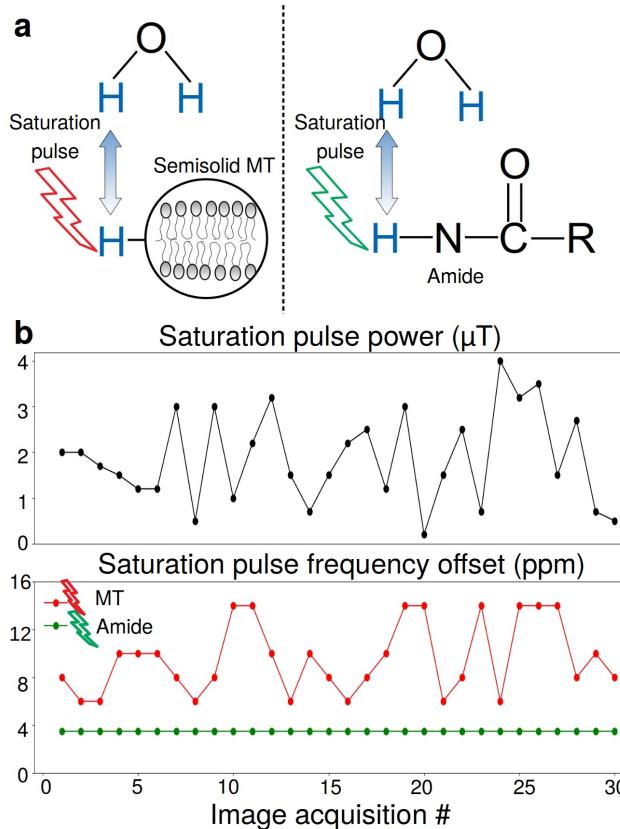


Cohen et al., *MRM.*, 2018

Perlman et al., *Nat. Biomed. Eng.*, 2022

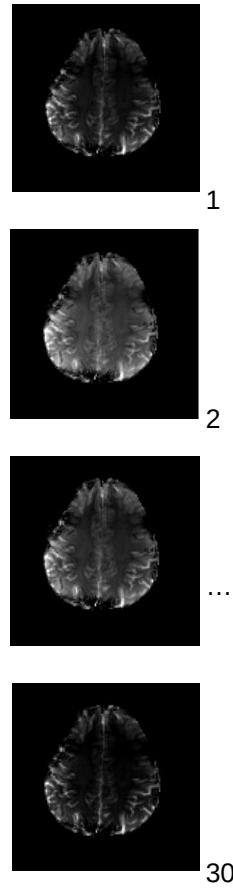
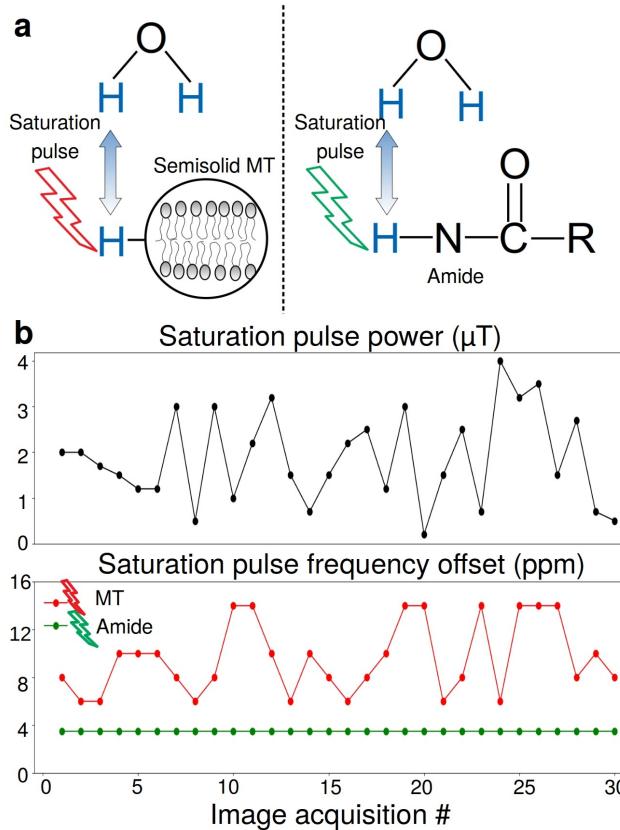
CEST MRF

Acquisition Schedule



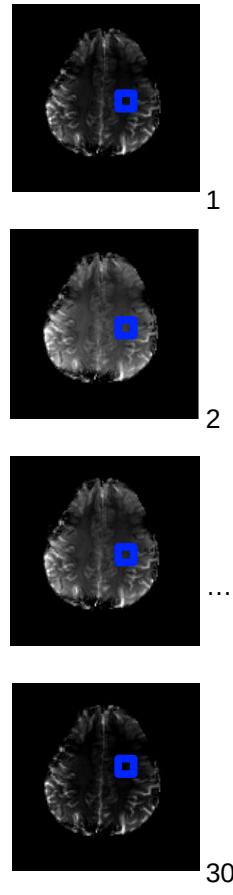
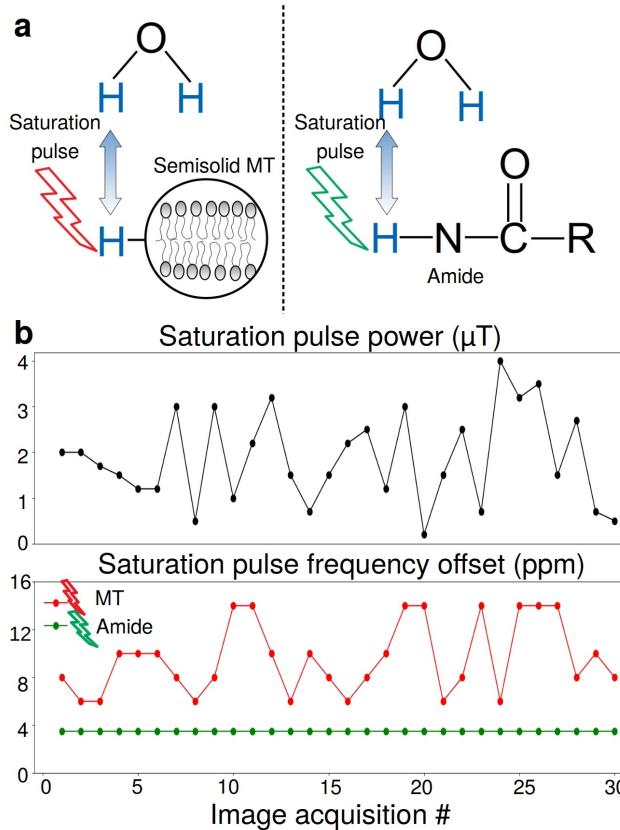
CEST MRF

Acquisition Schedule



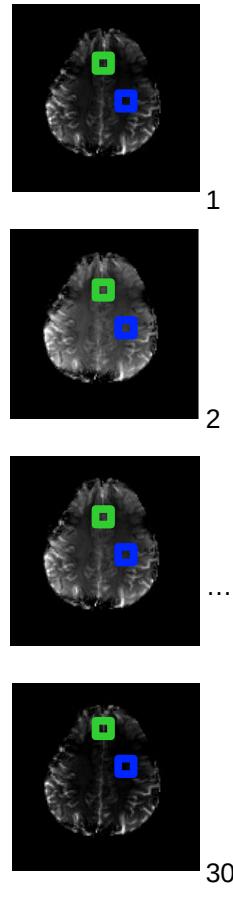
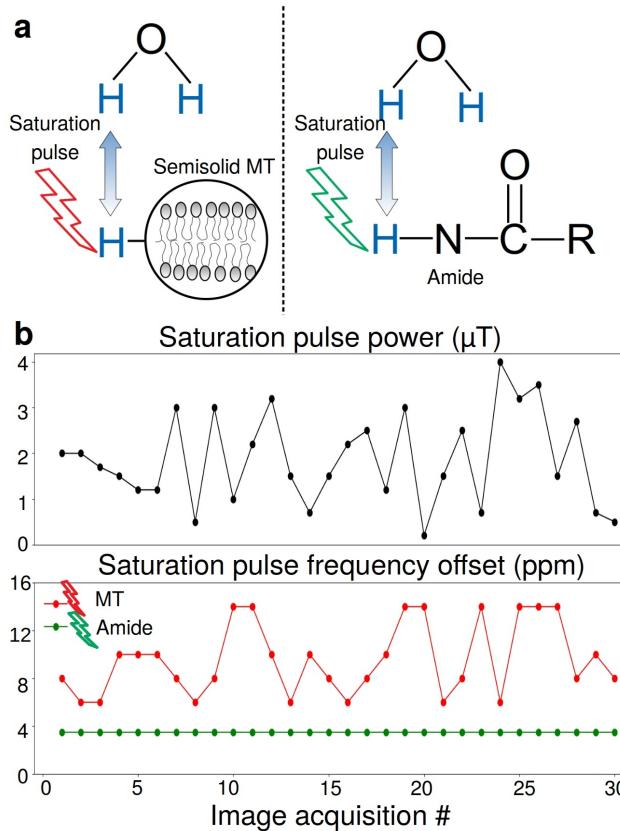
CEST MRF

Acquisition Schedule



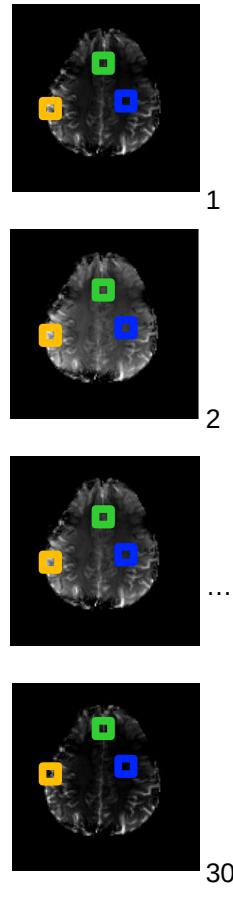
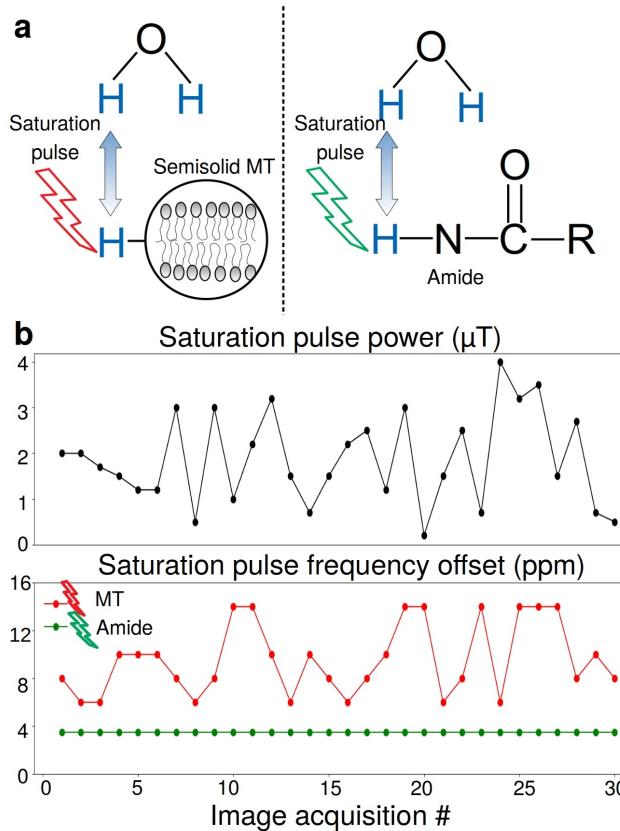
CEST MRF

Acquisition Schedule



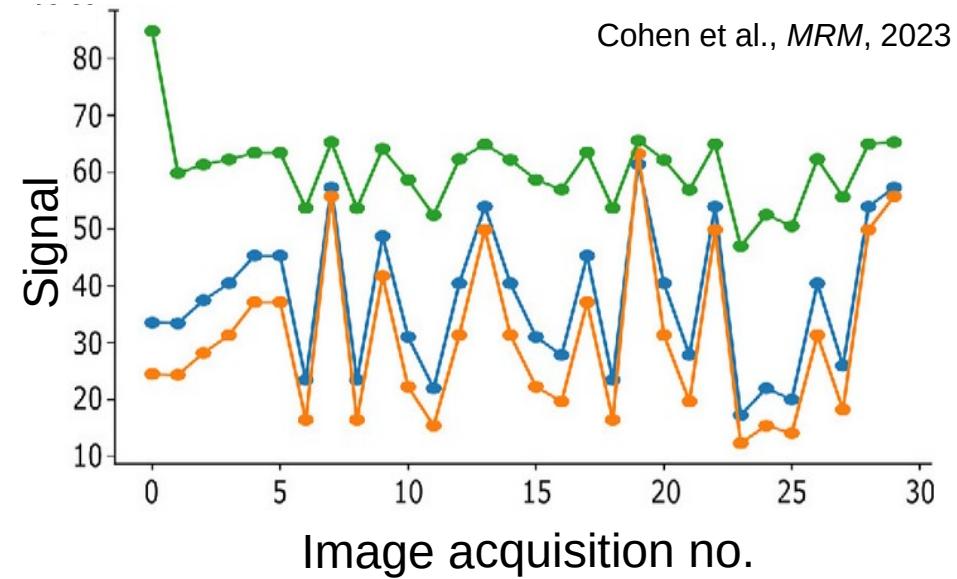
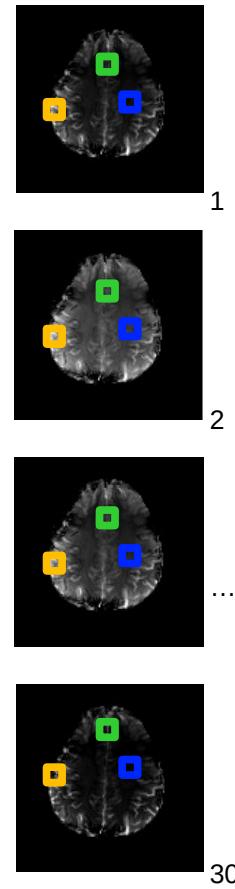
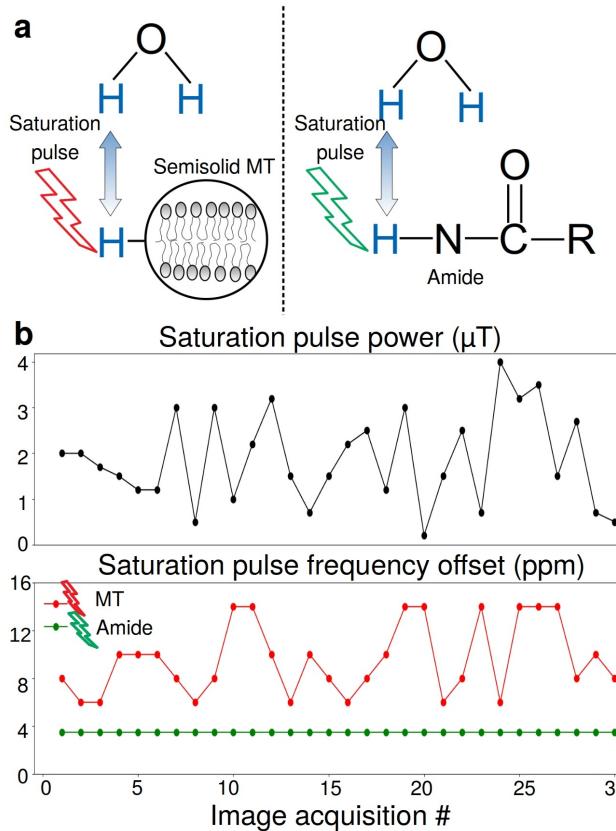
CEST MRF

Acquisition Schedule



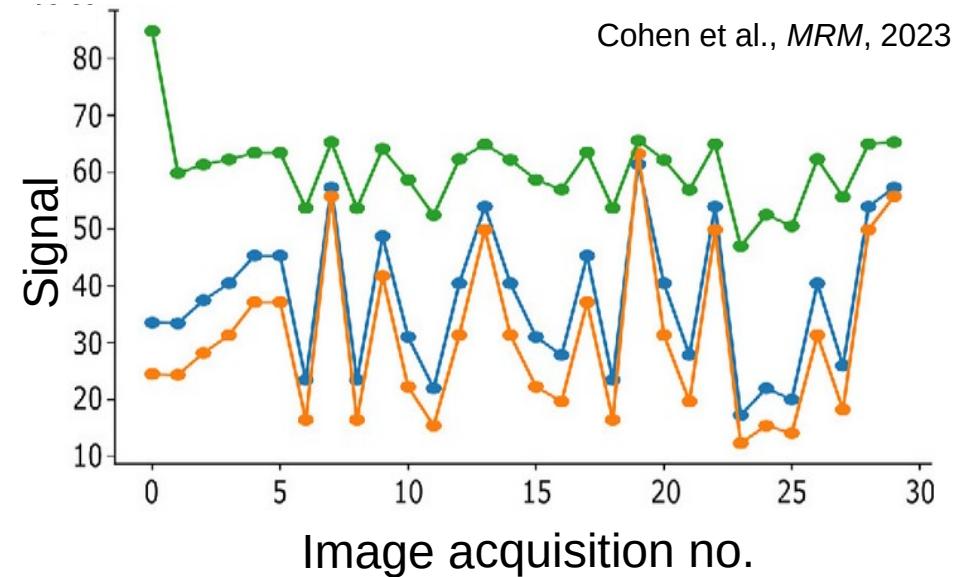
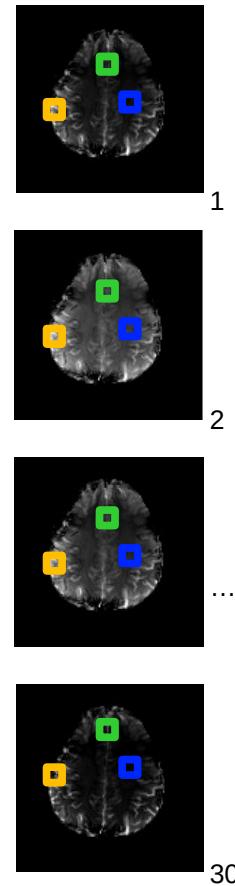
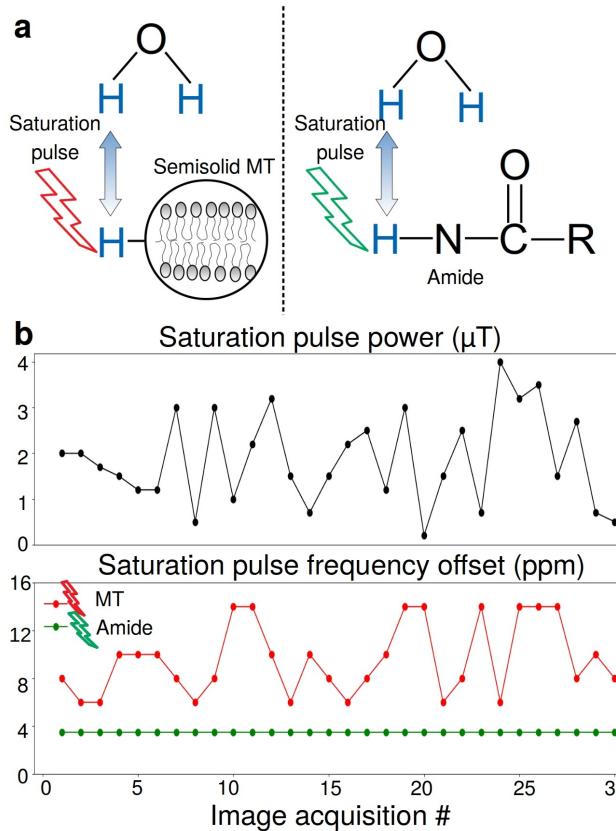
CEST MRF

Acquisition Schedule



CEST MRF

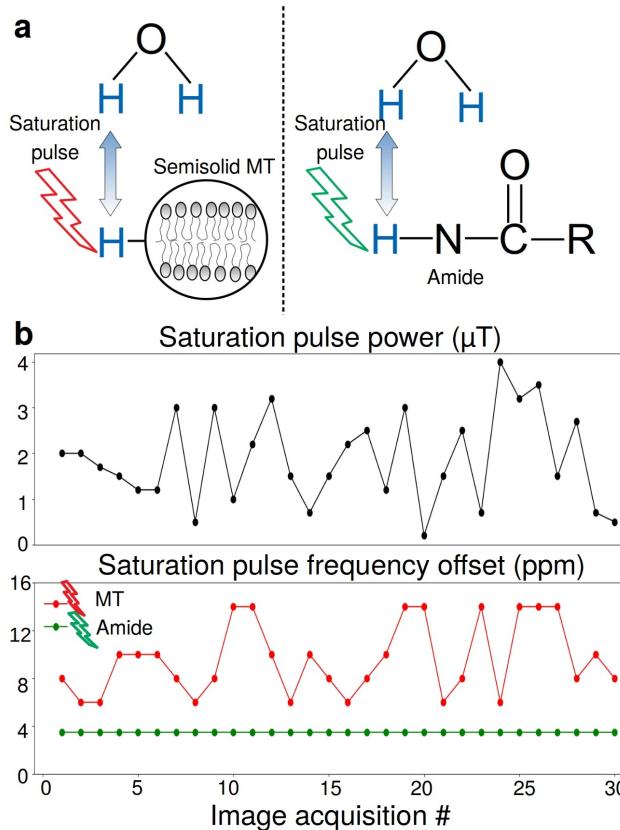
Acquisition Schedule



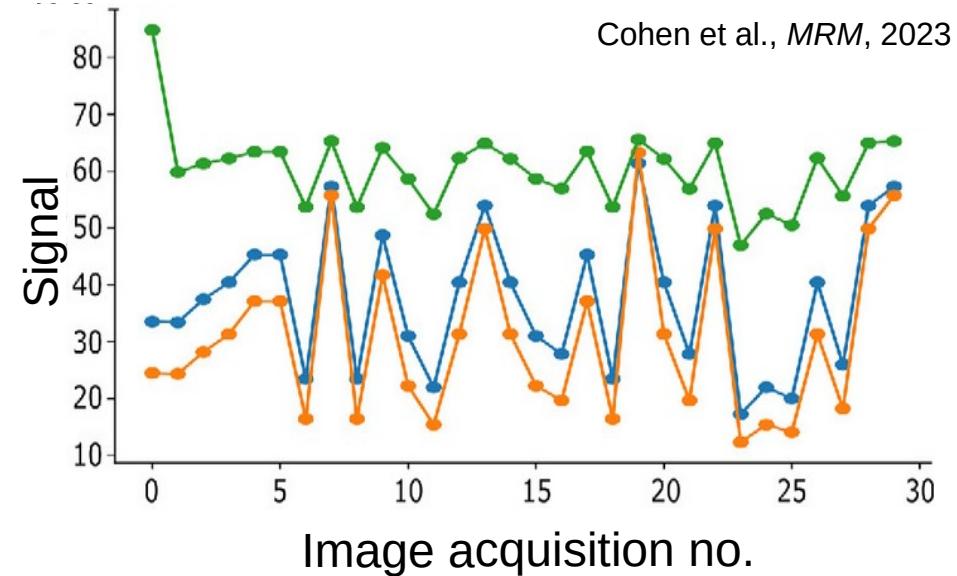
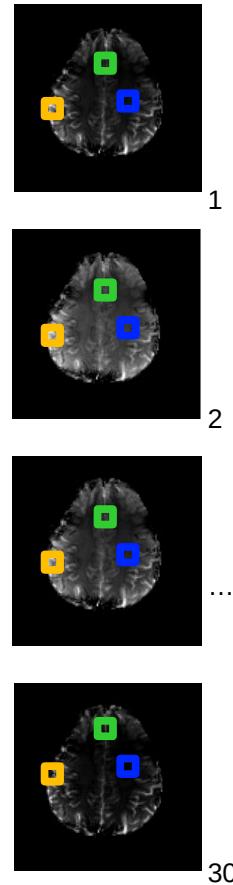
pH = 7.2 pH = 6.8 pH = 7.05
[NH] = 65 mM [NH] = 85 mM [NH] = 115 mM

CEST MRF

Acquisition Schedule



Perlman et al., *Nat. Biomed. Eng.*, 2022



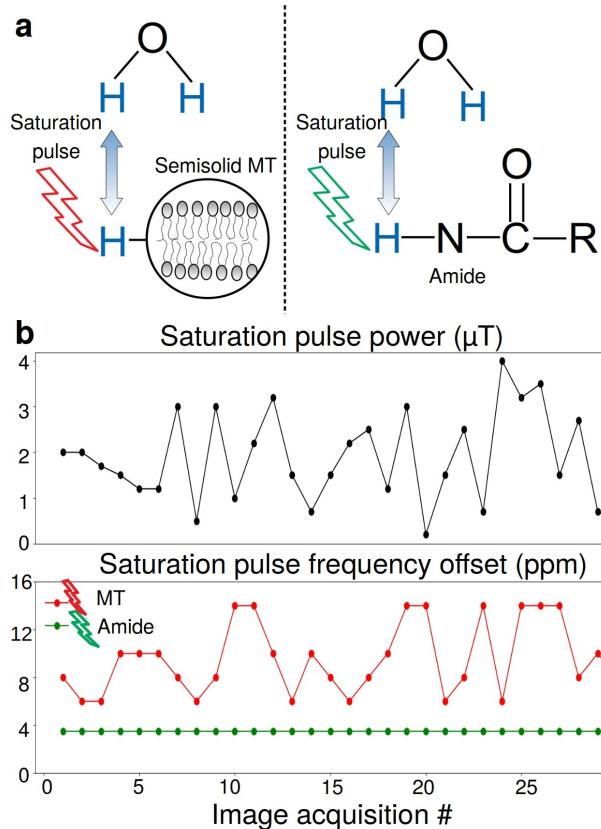
$$\frac{dM_x^s}{dt} = -R_{2s} M_x^s - \Delta\omega_s M_y^s + k_{ws} M_x^w - k_{sw} M_x^s$$

$$\frac{dM_y^s}{dt} = -R_{2s} M_y^s + \Delta\omega_s M_x^s + \omega_1 M_z^s + k_{ws} M_y^w - k_{sw} M_y^s$$

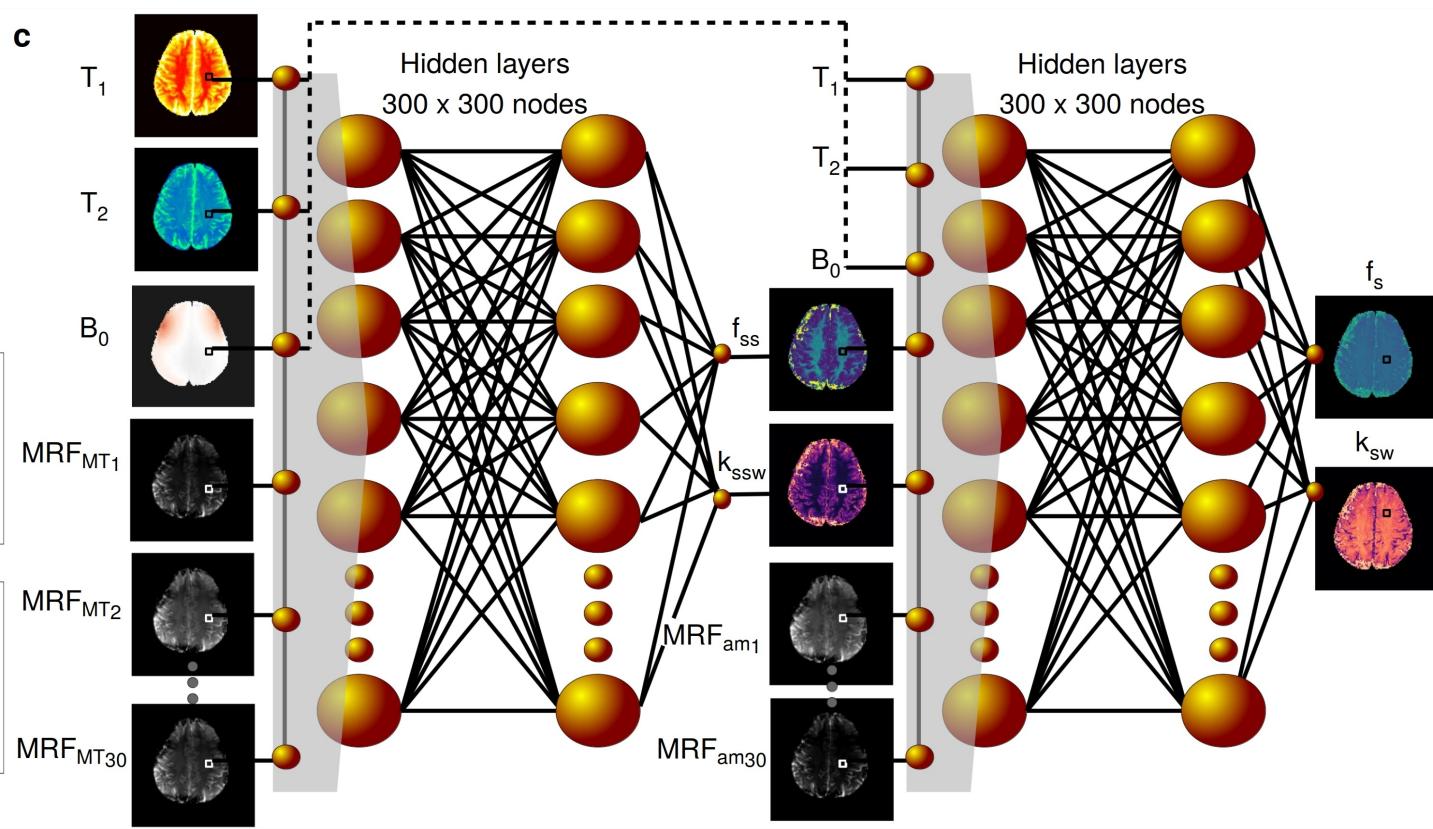
$$\frac{dM_z^s}{dt} = -R_{1s} M_z^s + R_1^w M_0^w - \omega_1 M_y^s + k_{ws} M_z^w - k_{sw} M_z^s$$

AI-Based Quantification – CEST Fingerprinting

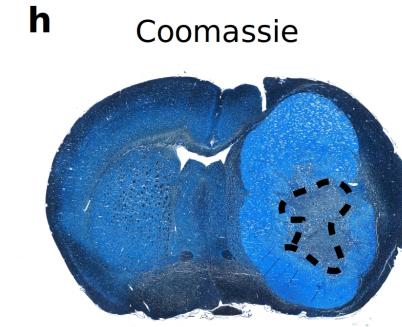
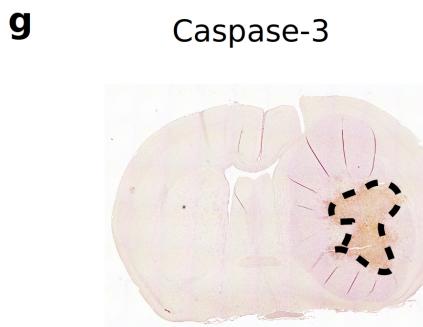
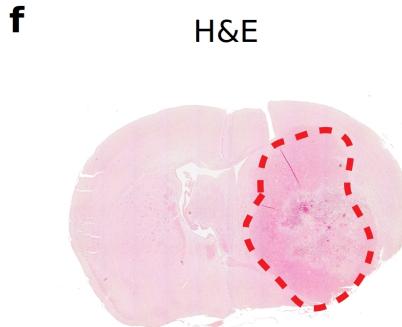
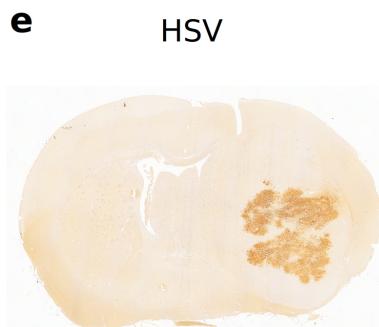
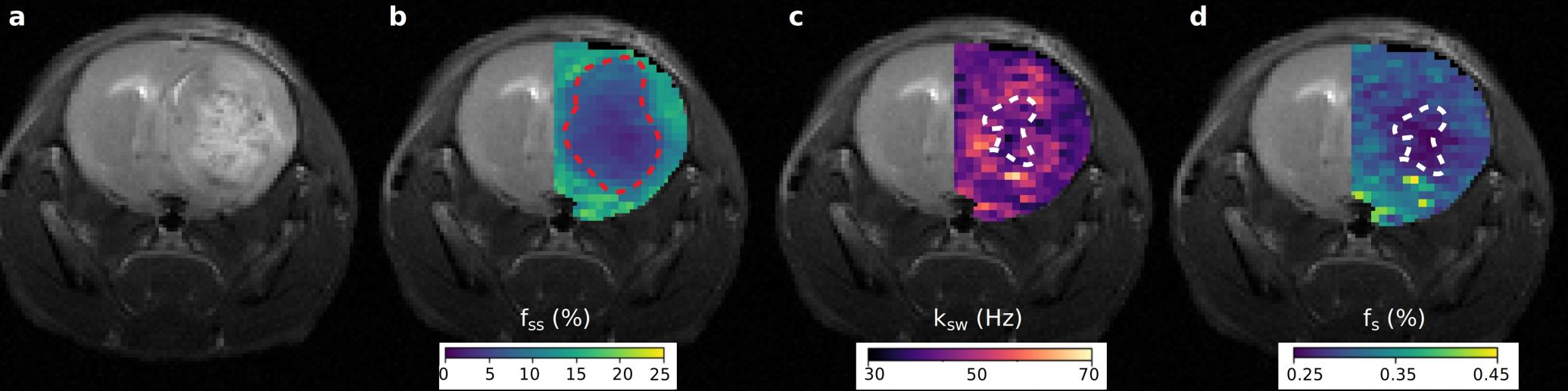
Acquisition Schedule



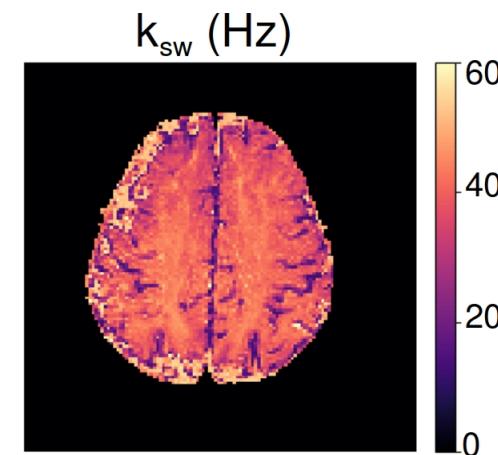
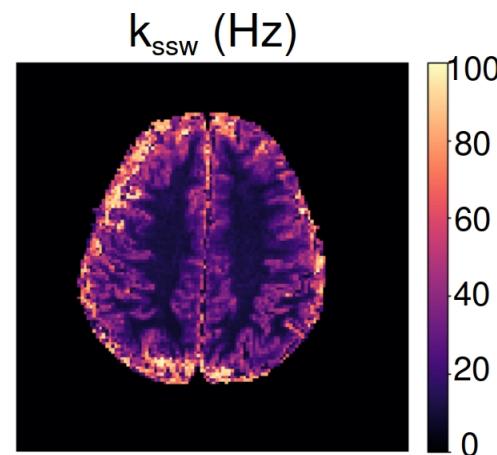
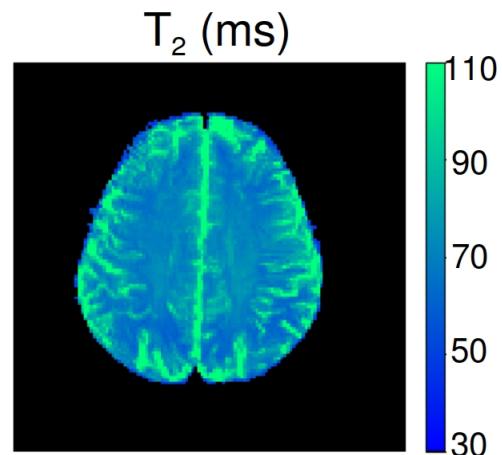
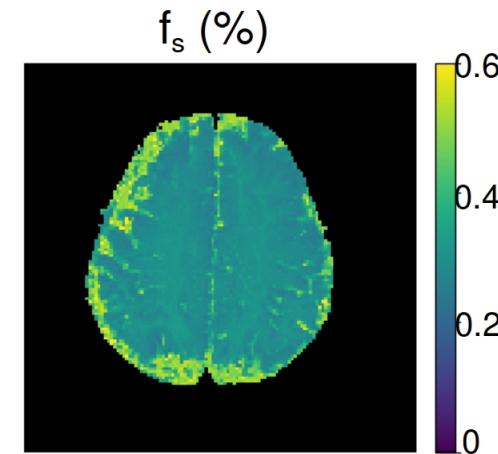
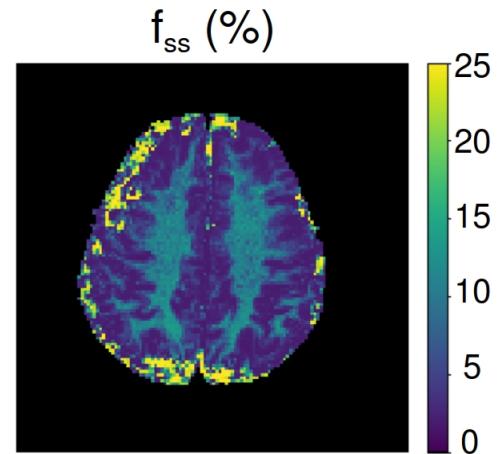
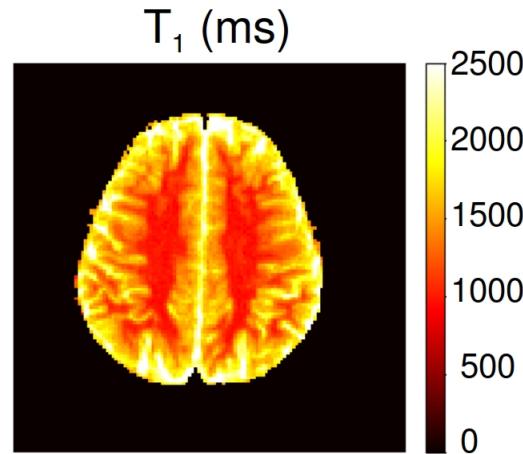
Deep Reconstruction Network



AI-Based Quantification – CEST/MT MRF



AI-Based Quantification – CEST/MT MRF

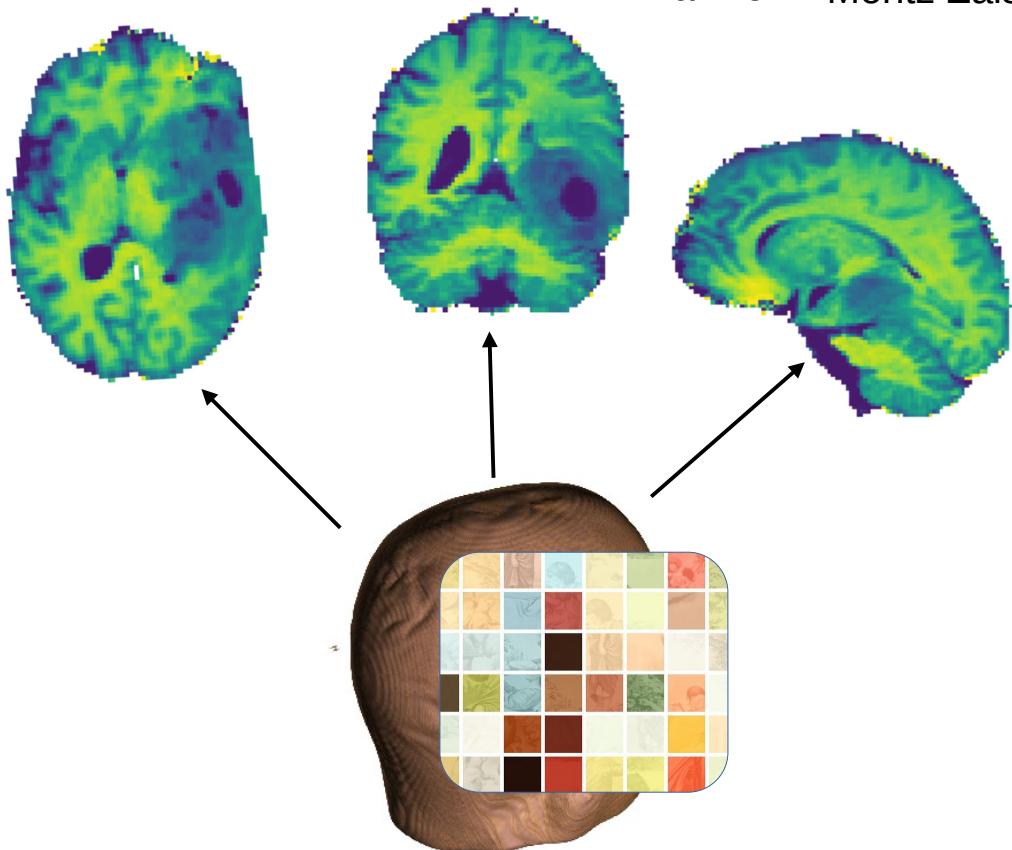


3D Whole Brain Molecular MRI



Kai Herz Moritz Zaiss

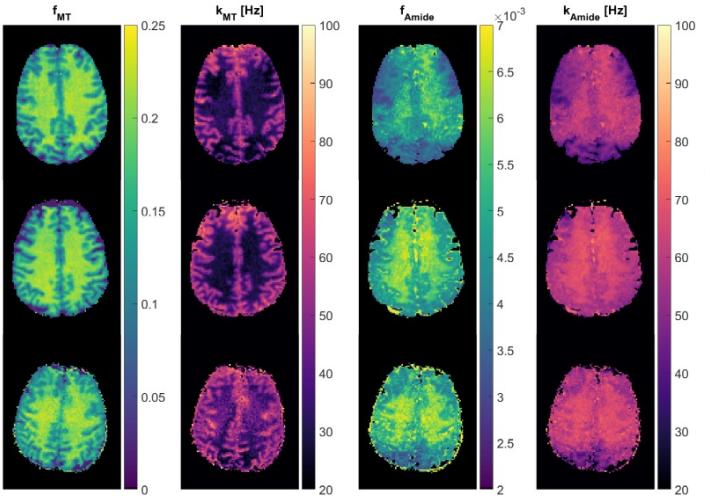
- Acq. Time for MT & amide: 5.5 min
- Full Acq. 11:09 min
- Reco. MT & amide: 2.5 sec
- Isotropic resolution: 1.8 mm



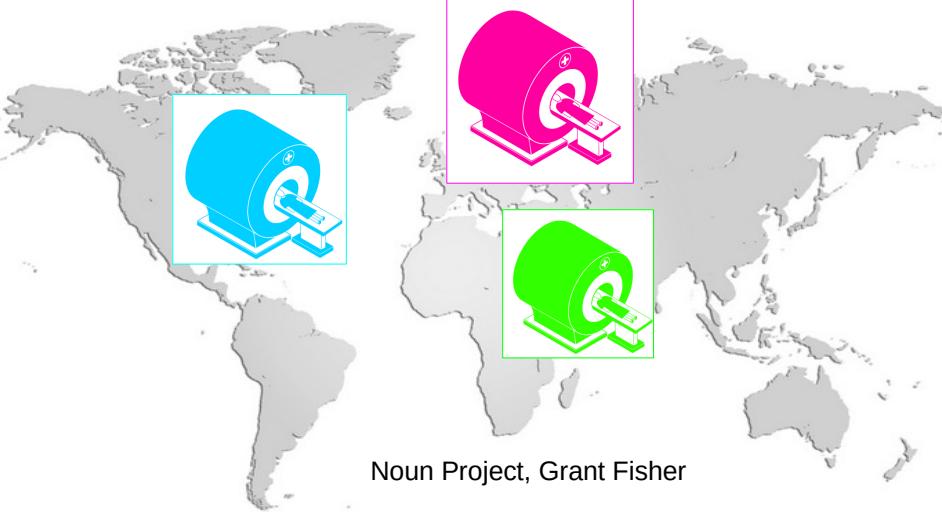
Reproducibility



Kai Herz Moritz Zaiss



Herz, Mueller, Perlman et al.
Magn Reson Med. 2021



Noun Project, Grant Fisher

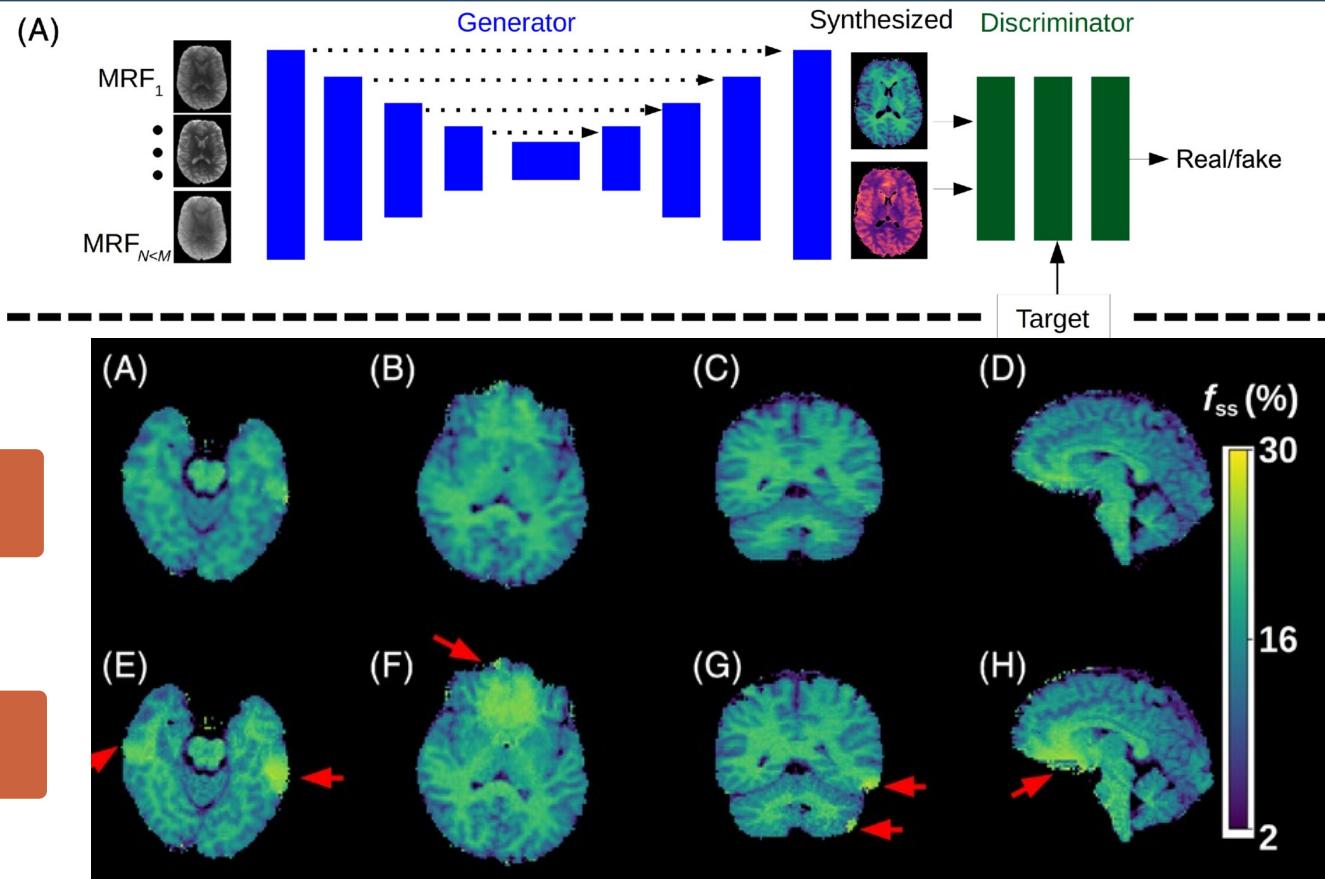
<https://pulseq-cest.github.io/>

| | f_{MT} GM (%) | k_{MT} GM [Hz] | f_{MT} WM (%) | k_{MT} WM [Hz] |
|-----------------|-----------------|------------------|-----------------|------------------|
| Tubingen Prisma | 14.0 ± 3.3 | 47.3 ± 10.8 | 20.1 ± 1.7 | 31.7 ± 6.66 |
| Boston Prisma | 14.2 ± 3.8 | 47.7 ± 11.3 | 20.3 ± 1.9 | 32.0 ± 6.58 |
| Erlangen Trio | 14.2 ± 3.4 | 48.6 ± 11.2 | 19.7 ± 2.2 | 35.2 ± 8.57 |

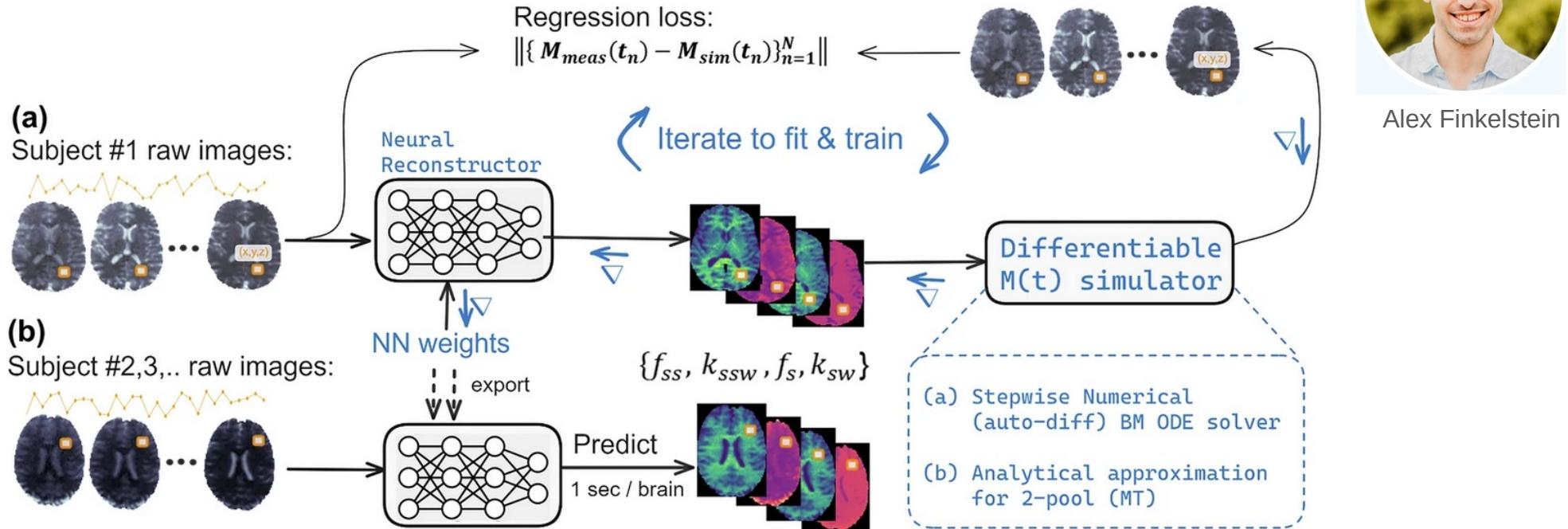
Denoising



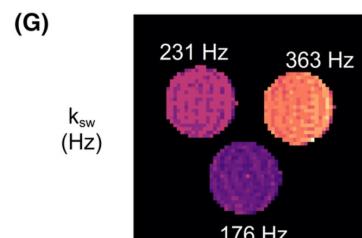
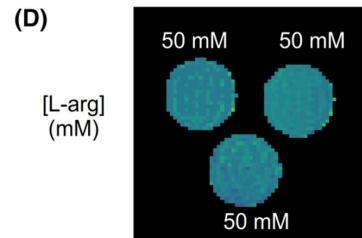
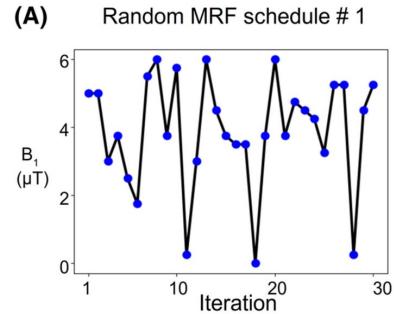
Jonah Weigand-
Whittier



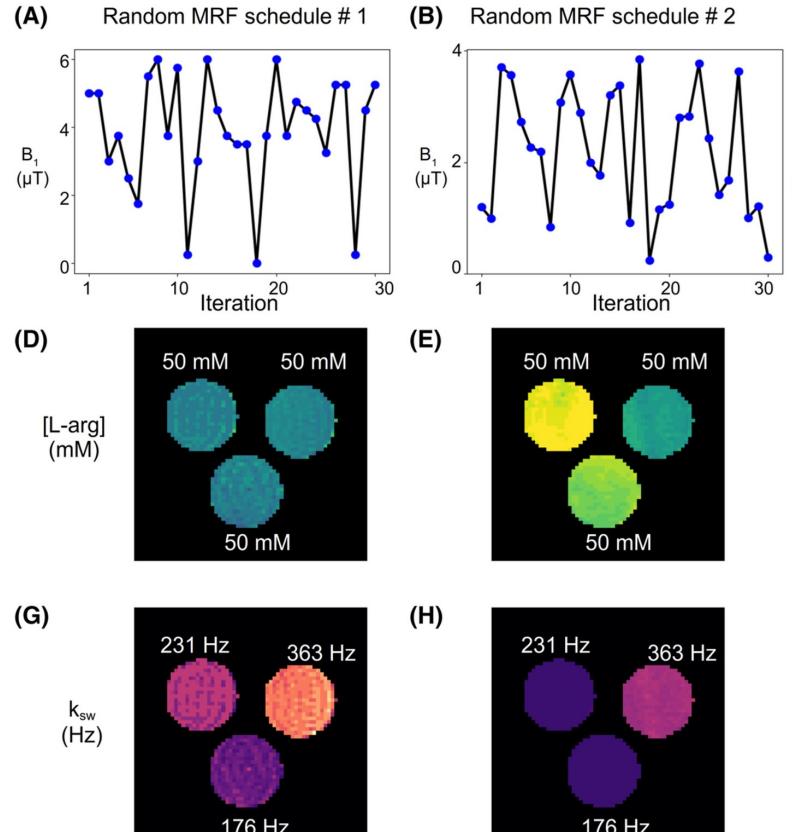
Circumvent Dictionaries & Improve Consistency



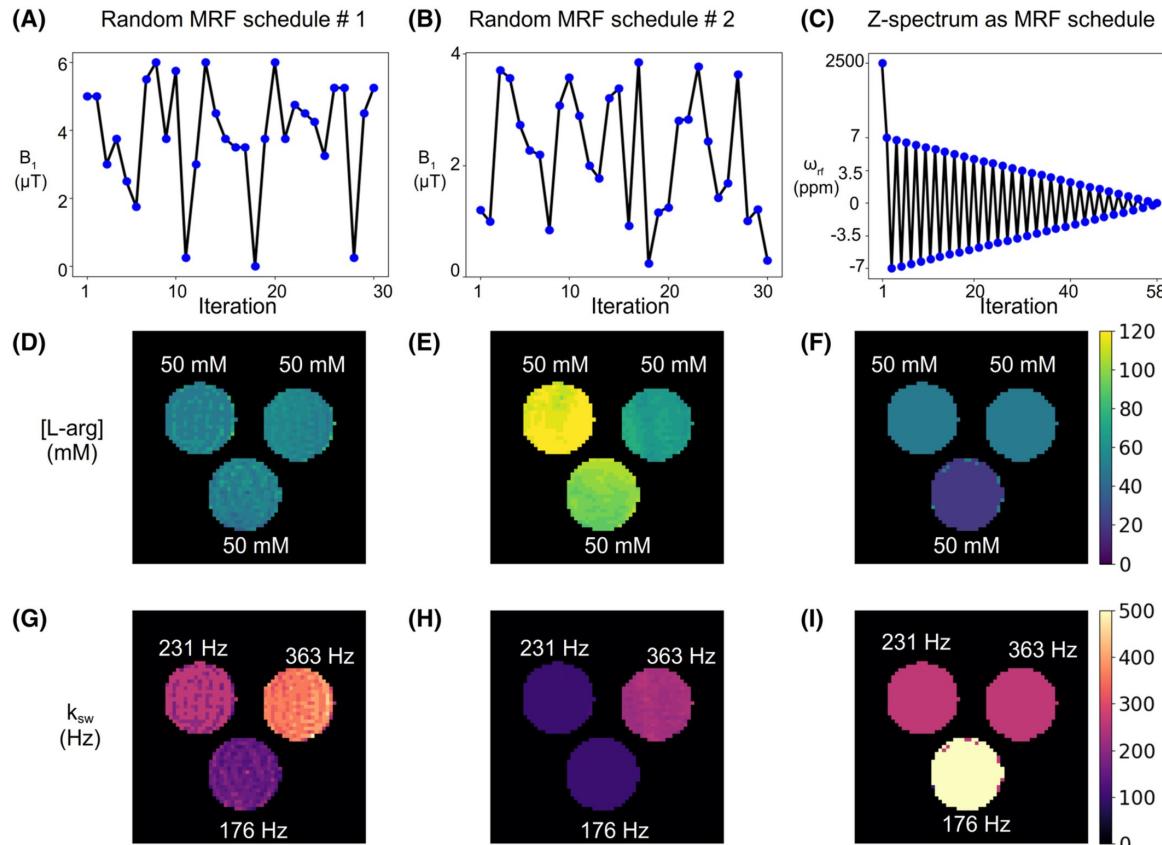
Optimal Acquisition Pattern?



Optimal Acquisition Pattern?



Optimal Acquisition Pattern?



Auto-Discover Molecular Imaging Protocols

Flip Angle

Saturation Duration

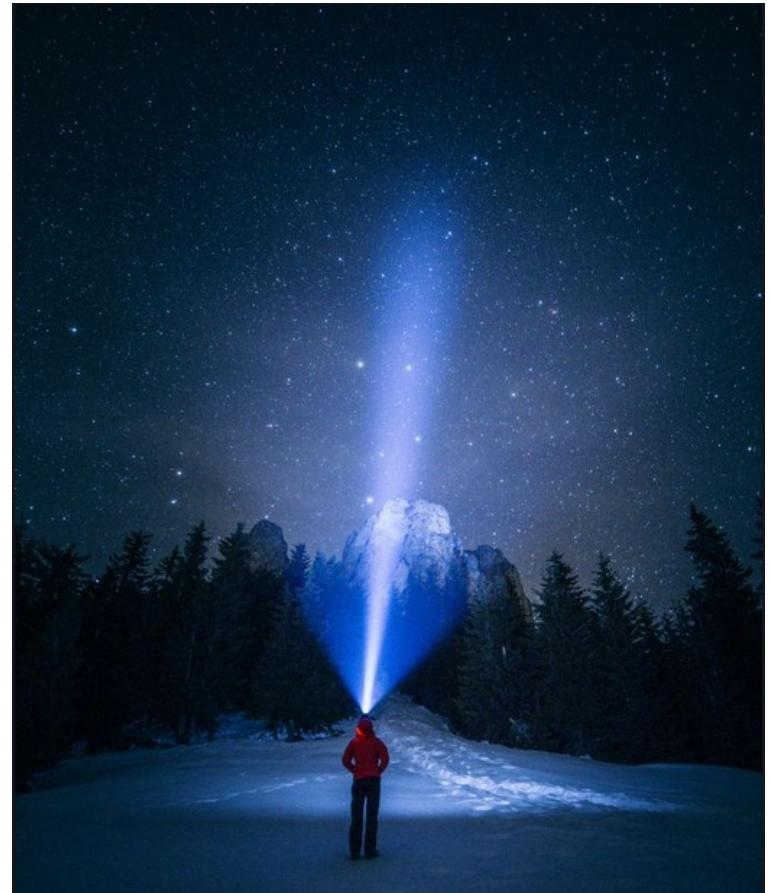
Repetition Time

Optimal Acquisition Protocol?

Saturation Pulse Power

Echo Time

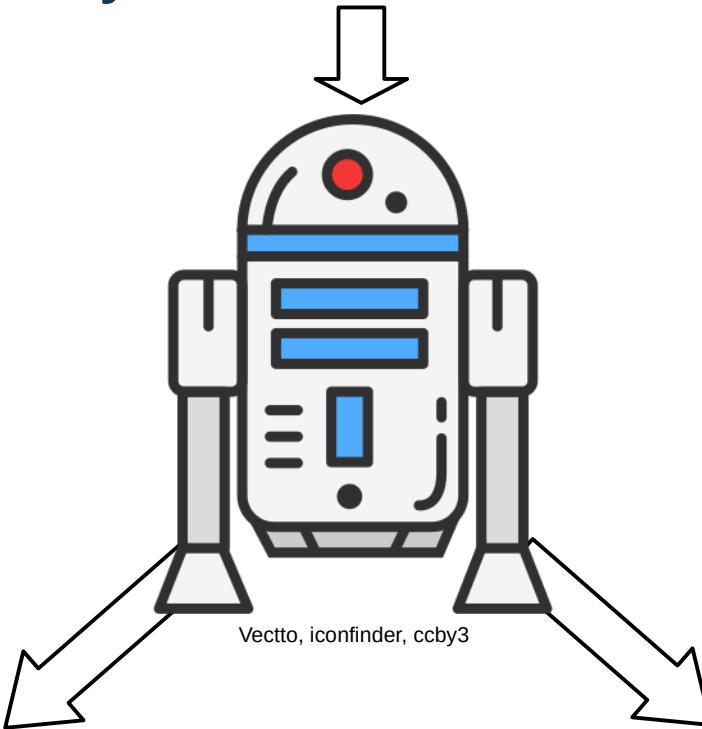
Saturation Pulse Frequency Offset



Noun Project, Szabo Edwin-Edward

Auto-Discover Molecular Imaging Protocols

Broadly defined CEST scenario

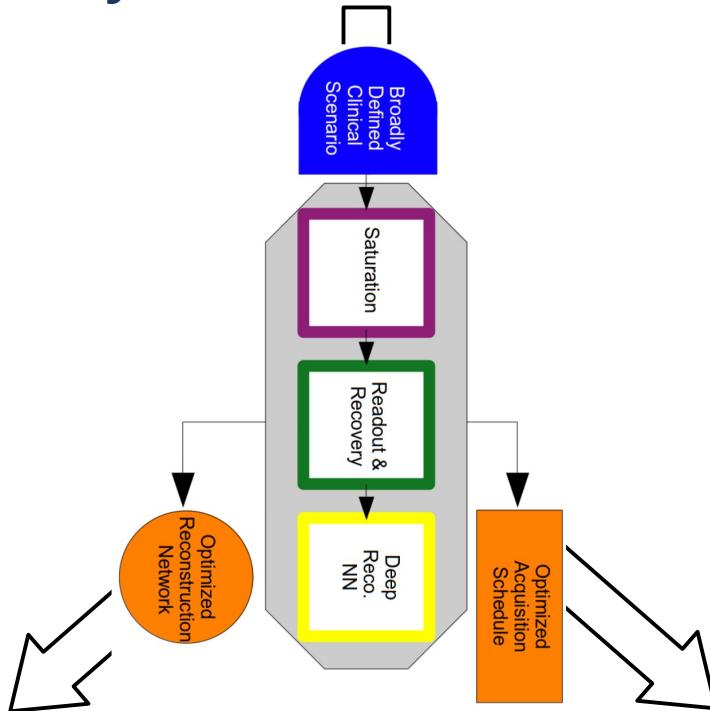


Optimal acquisition schedule

Optimal reconstruction NN

Auto-Discover Molecular Imaging Protocols

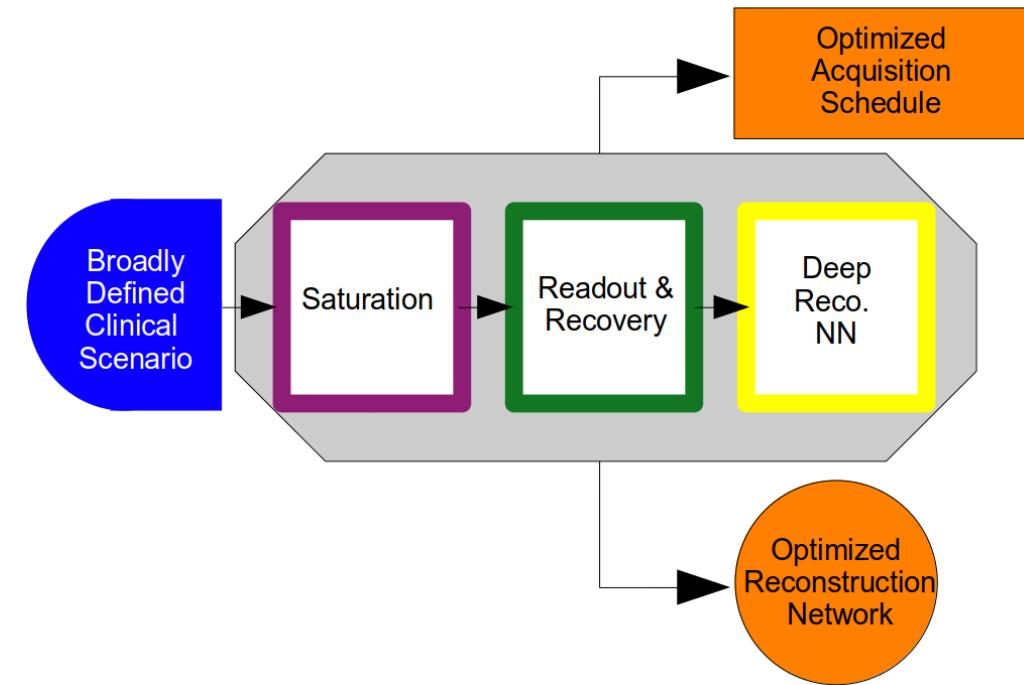
Broadly defined CEST scenario



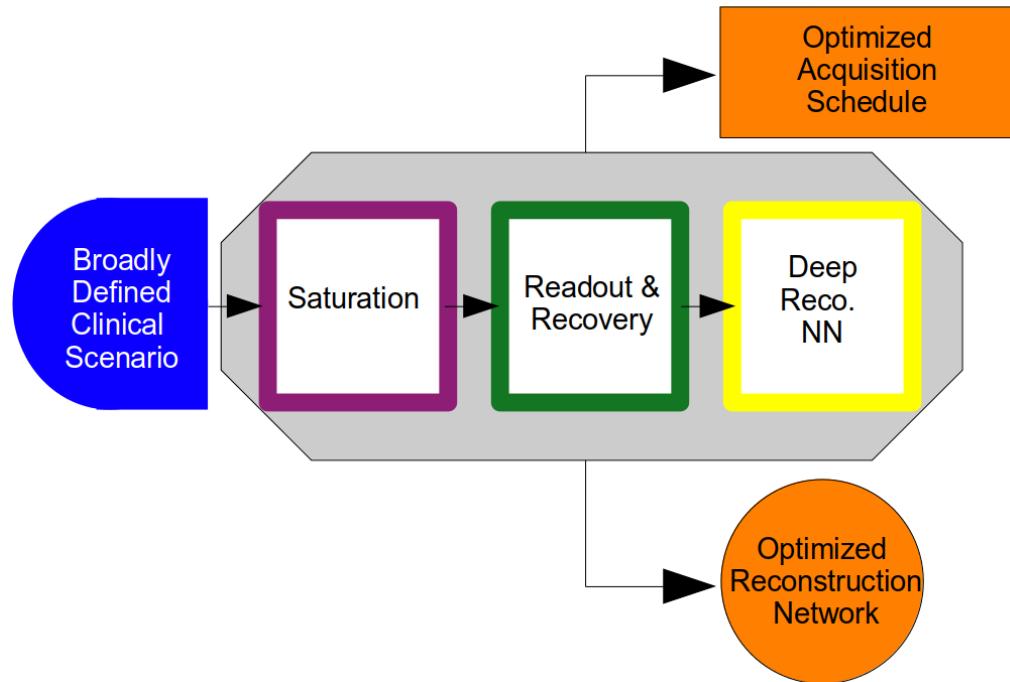
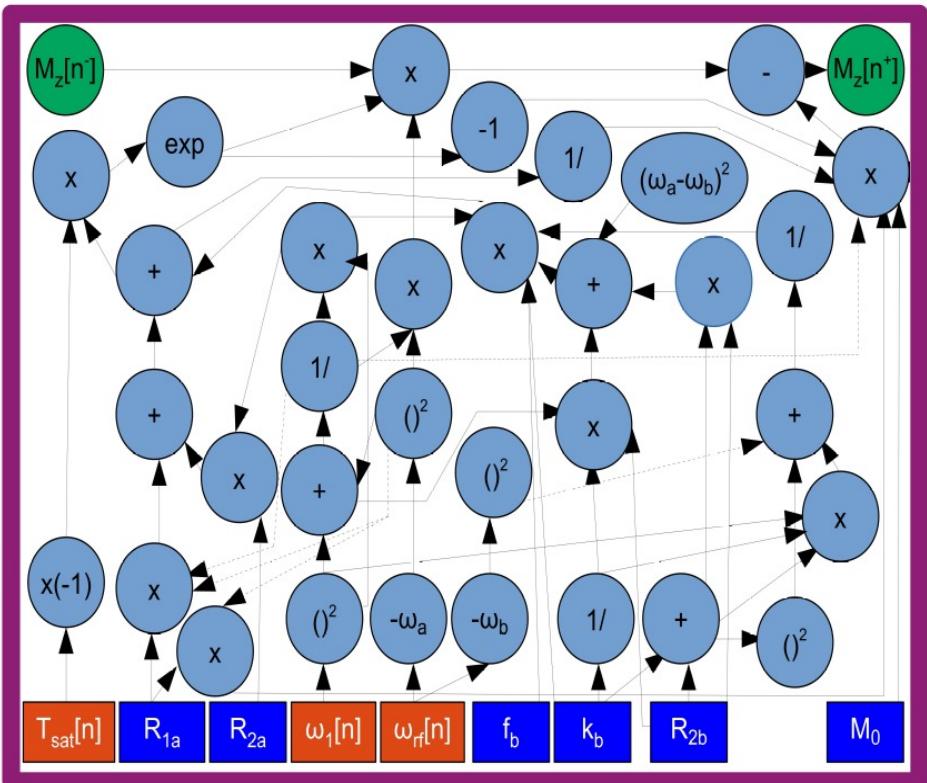
Optimal acquisition schedule

Optimal reconstruction NN

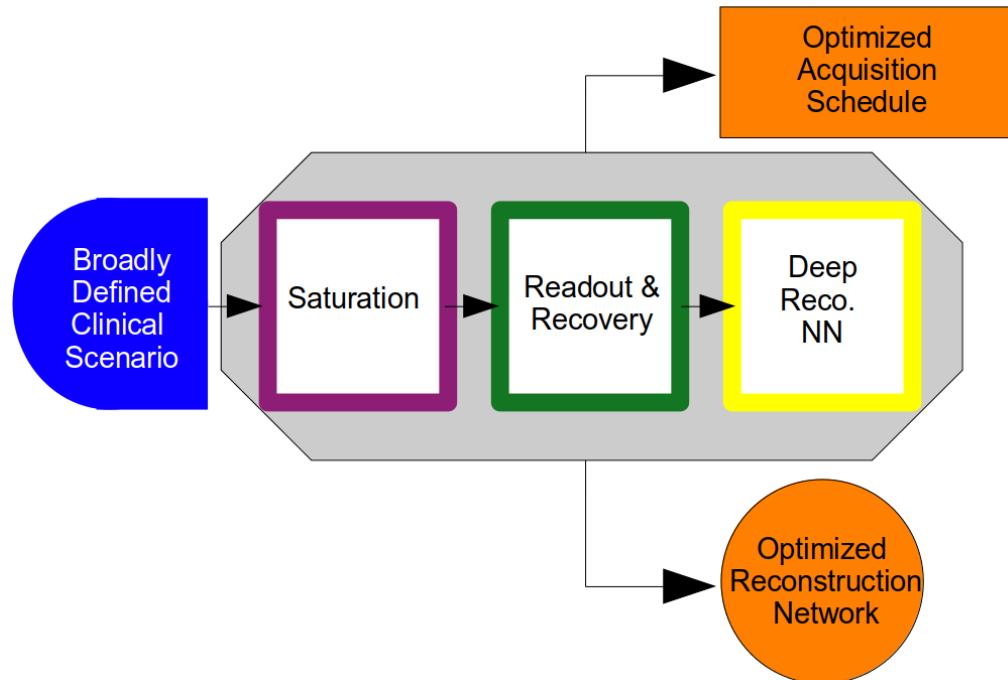
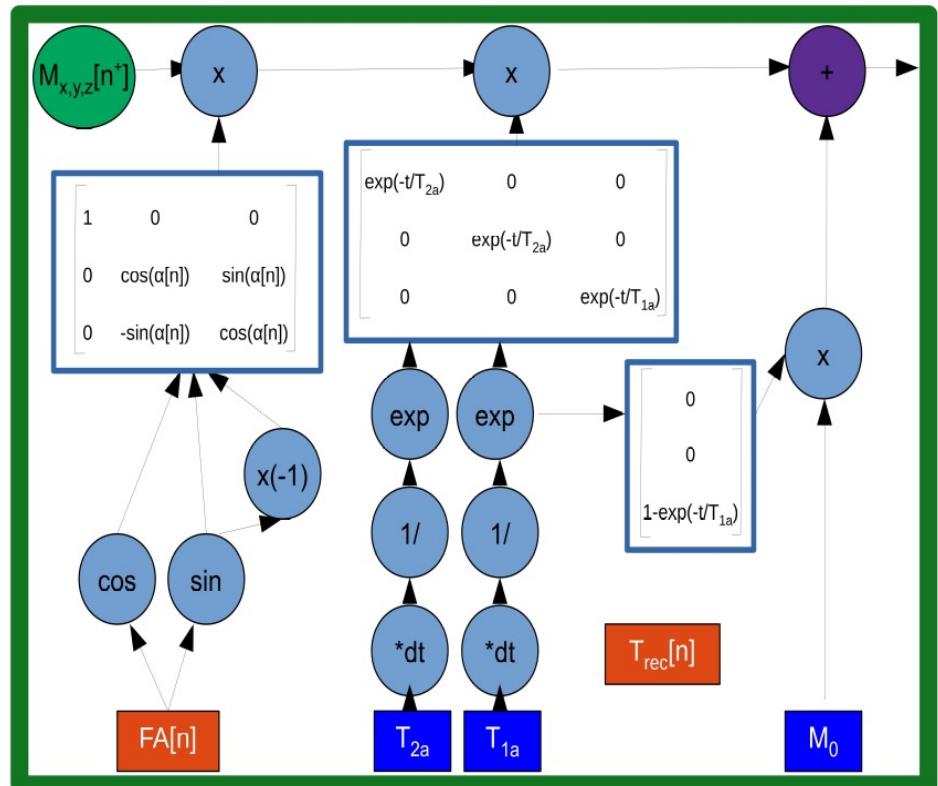
Auto-Discover Molecular Imaging Protocols



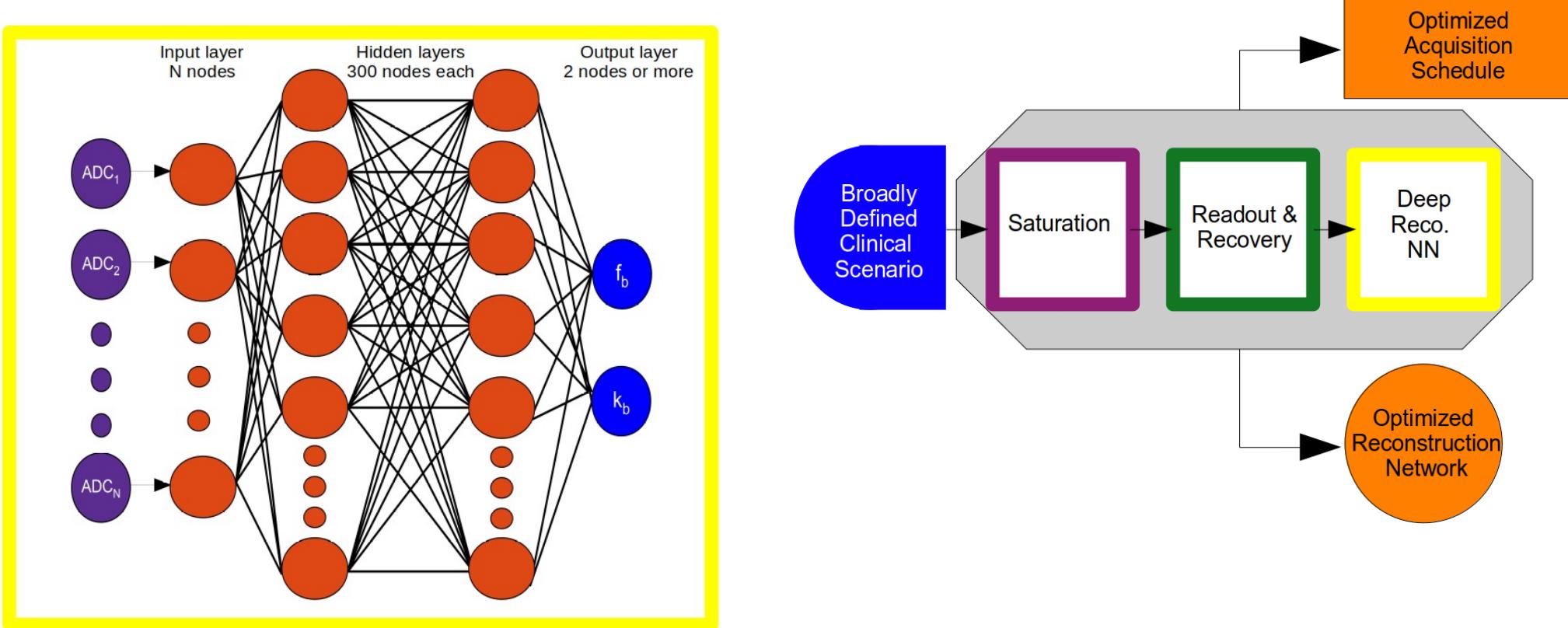
Auto-Discover Molecular Imaging Protocols



Auto-Discover Molecular Imaging Protocols

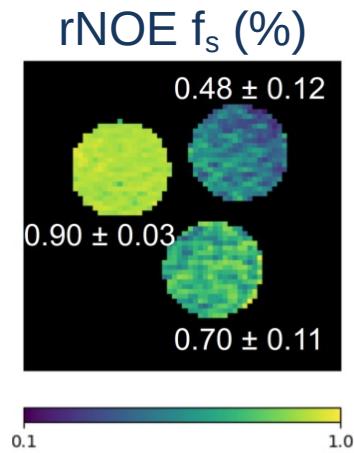
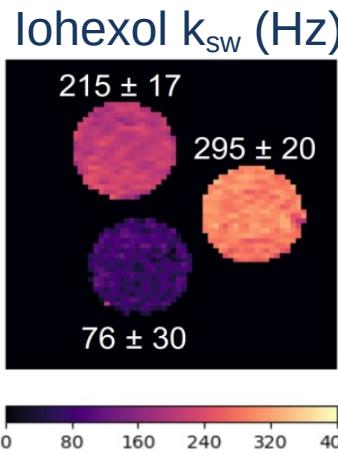
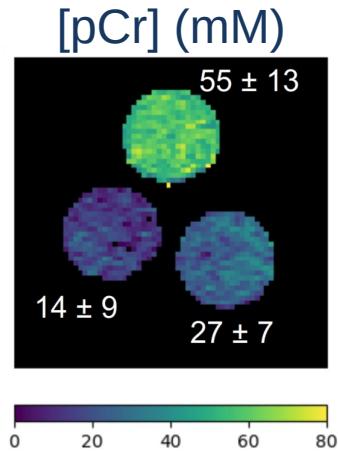


Auto-Discover Molecular Imaging Protocols

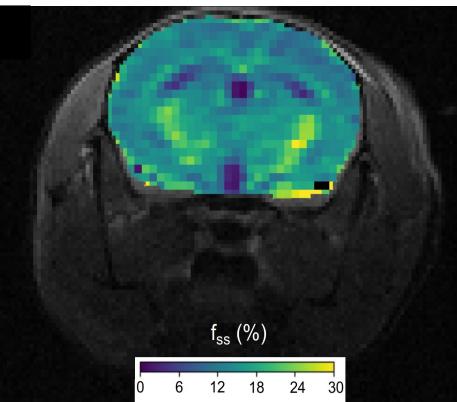
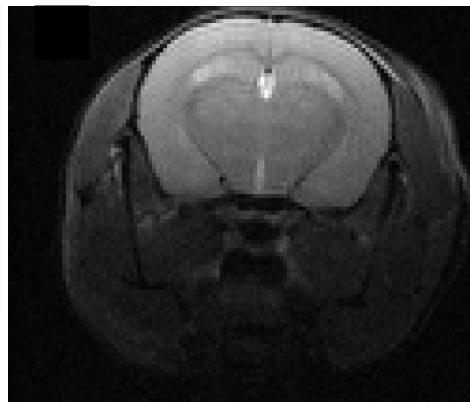
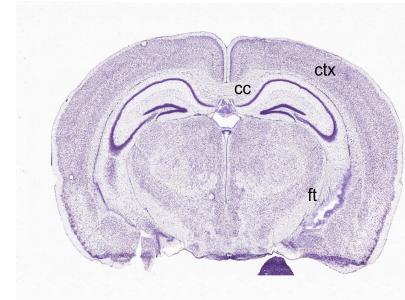


Auto-Discover Molecular Imaging Protocols

Acquisition time
35 - 71s



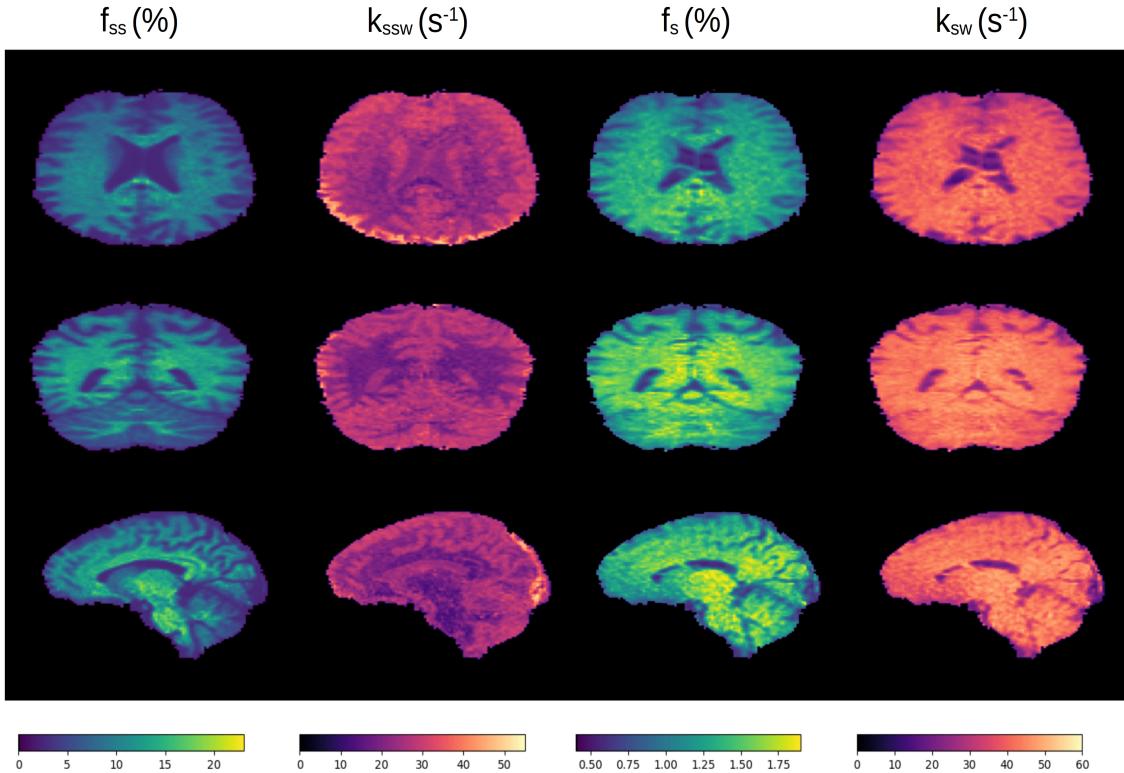
Parameter quantification time
29 ms



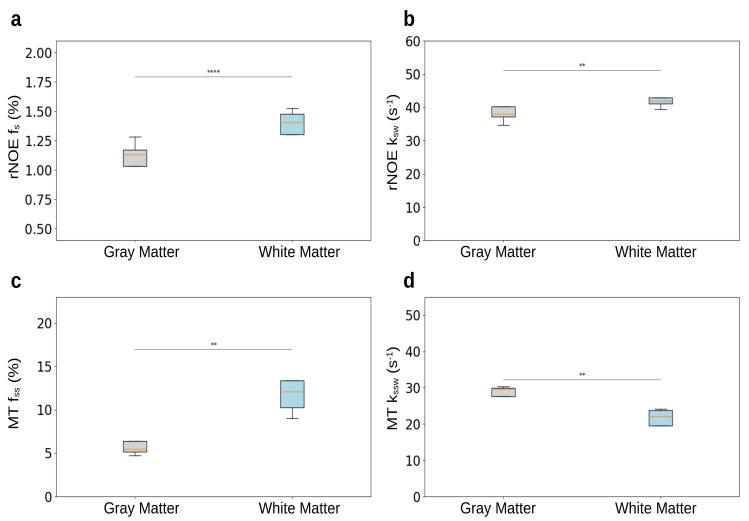
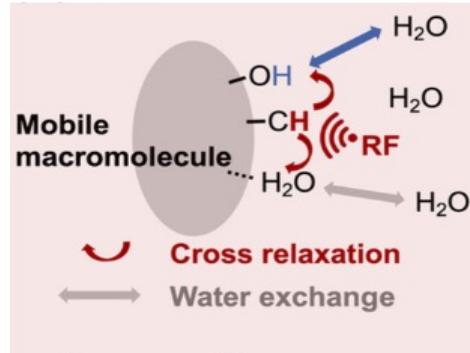
Extension for Other Contrast Mechanisms



Inbal Power



Power et al., *iScience* 2024

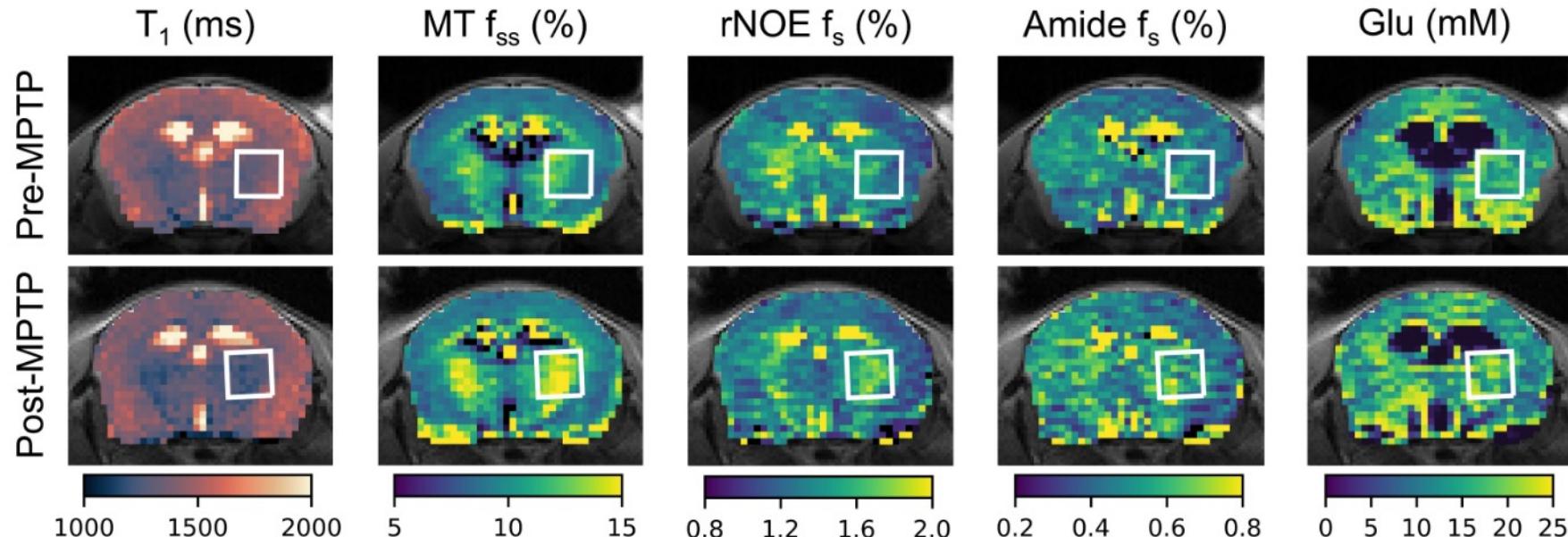


Extension for Other Contrast Mechanisms



Quantification of Glutamate, Mobile Proteins & Semisolid Macromolecules in a Mouse Parkinson's Model

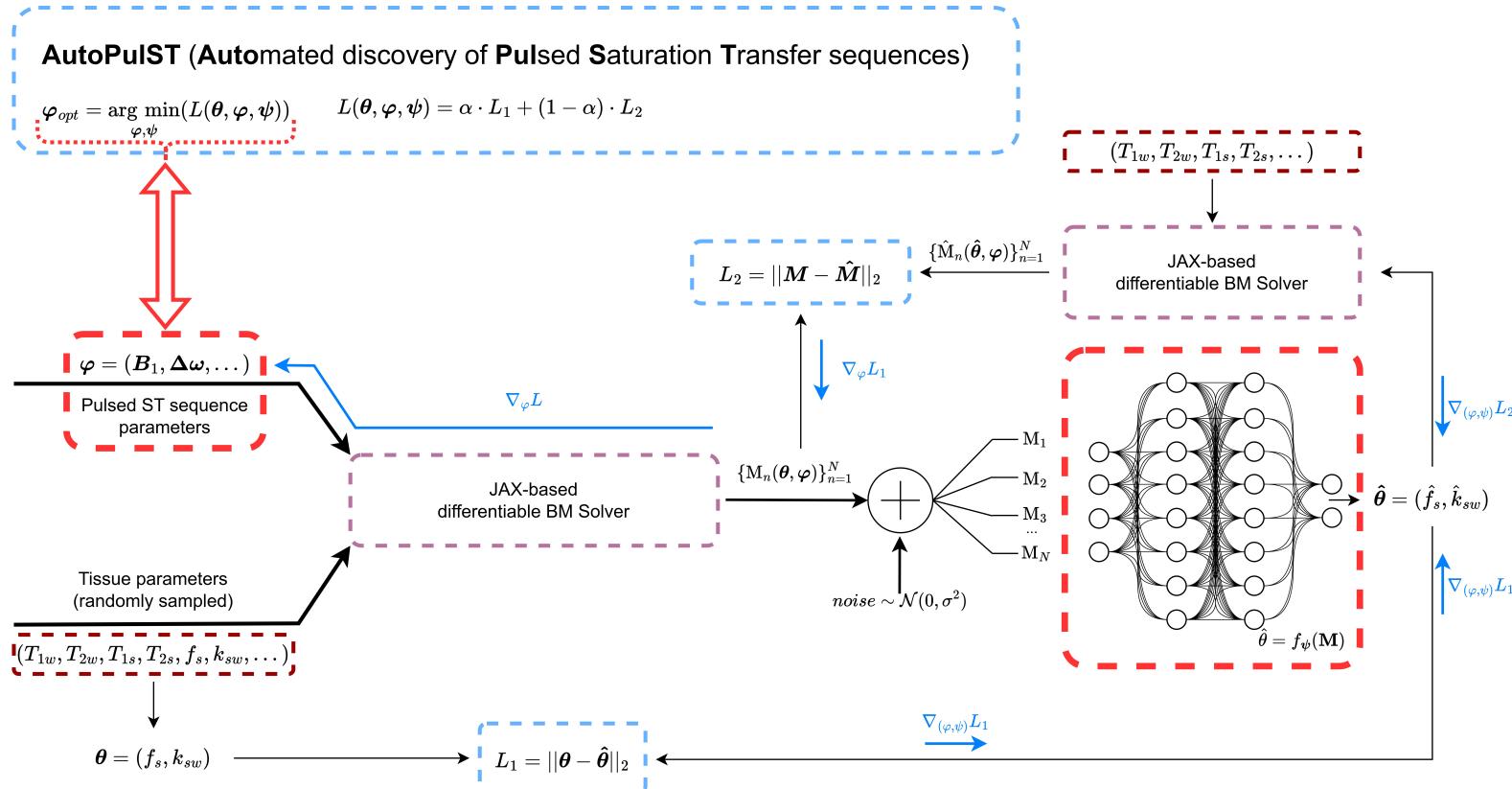
Hagar Shmueli



Addressing Pulsed Saturation



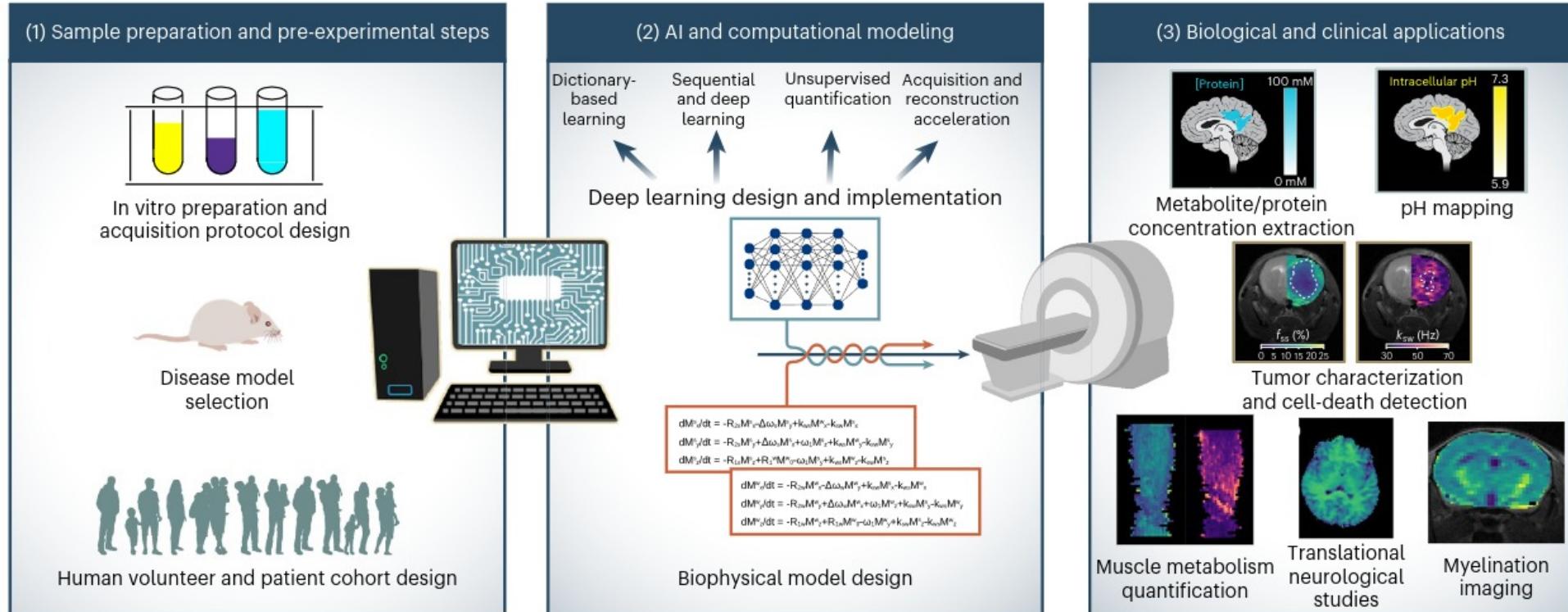
Nikita Vladimirov



Complete Protocol & Open Code



Nikita Vladimirov



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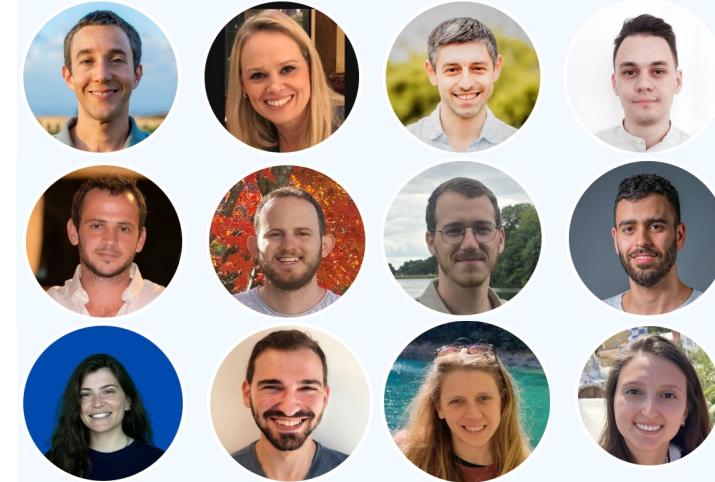
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