



University of California
San Francisco

Imaging Strategies: Sequences & Trajectories

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*University of Aarhus Training course on Hyperpolarized ^{13}C &
 ^{129}Xe MRI: moving to clinical use*

October 8, 2026

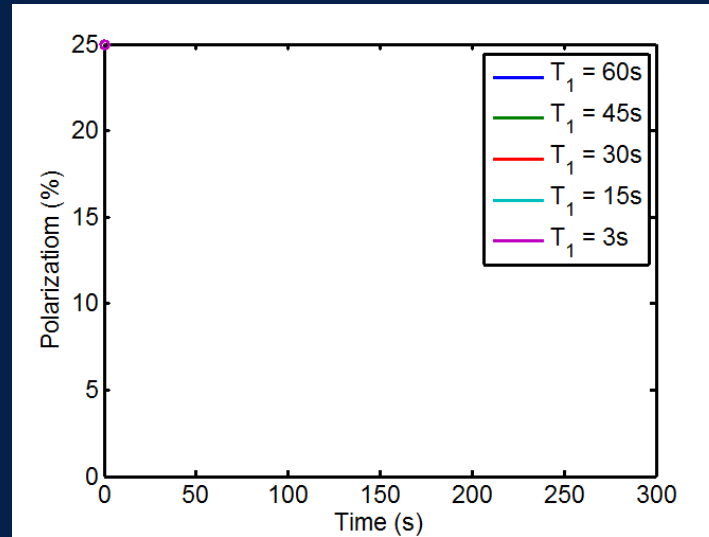
Learning Objectives

1. Describe the challenges associated with HP ^{13}C MRI
2. Understand the basic and advanced acquisition strategies for HP ^{13}C MRI
3. Balance the tradeoffs between the different imaging approaches

Challenges: Non-Renewable Magnetization (T_1 Decay)

$$S(t) \propto \exp(-t/T_1)$$

<5% signal after $3T_1$



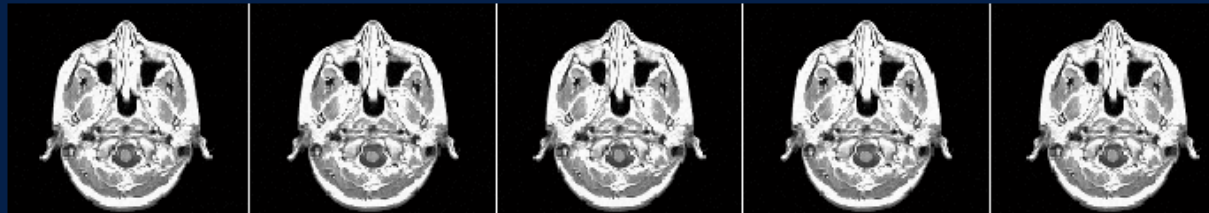
$T_1 = 3s$

$T_1 = 15s$

$T_1 = 30s$

$T_1 = 45s$

$T_1 = 60s$



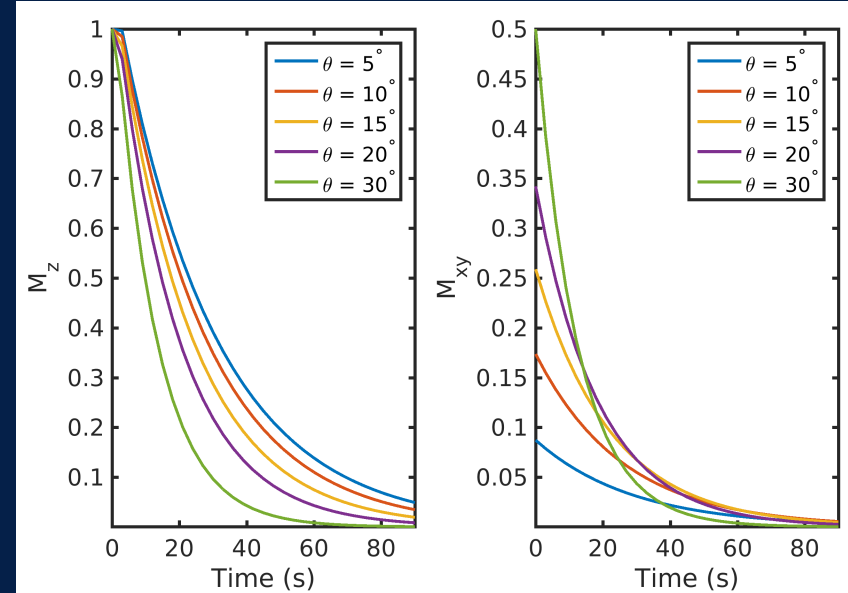
Challenges: Non-Renewable Magnetization (RF Effects)

- ^1H MRI: θ chosen to provide contrast or maximize signal
- HP MRI: RF pulses effectively 'consume' magnetization:

$$M_Z(t) = M_{Z,HP} \exp\left(-\frac{t}{T_1}\right) \cos^n \theta$$

$$M_{XY}(t) = M_{Z,HP} \exp\left(-\frac{t}{T_1}\right) \cos^{n-1} \theta \sin \theta$$

- Fundamental tradeoffs between SNR and total imaging time
 - Low flip $\rightarrow$ Preserve M_Z , but smaller M_{xy}
 - High flip $\rightarrow$ Consume M_Z , higher M_{xy} (initially), but faster decay



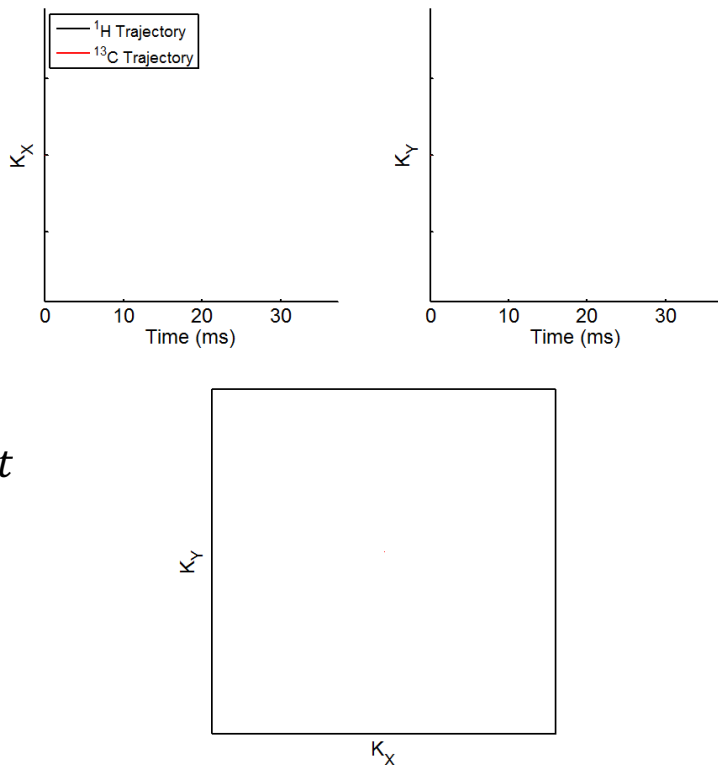
- Slice thickness and k-space trajectory modulated by γ :

$$\text{Slice Thickness: } BW / \gamma G_{sl}$$

$$\text{K-space Trajectory: } \gamma \int G_r(t) dt$$

$$\text{FOV: } 1 / \Delta k$$

$$\text{Resolution: } 1 / 2k_{\max}$$



- Due to differences in γ , for the same trajectory ¹³C images have:
 - 4X larger FOV
 - 4X coarser resolution
 - 4X thicker slice

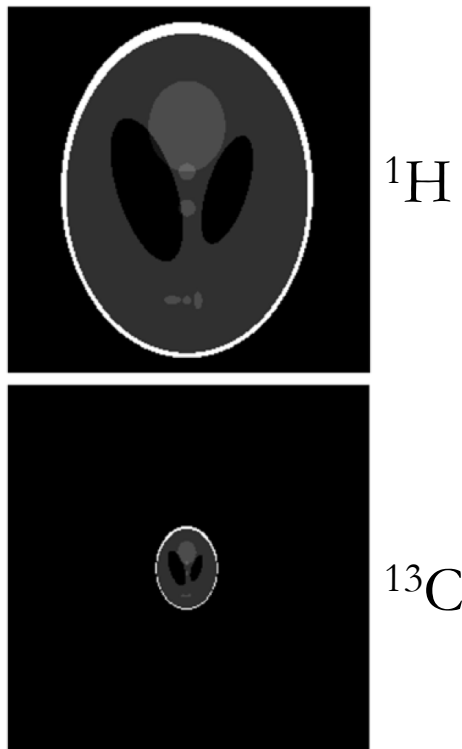
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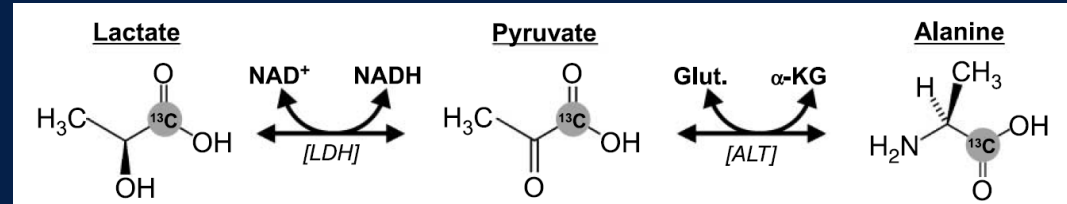
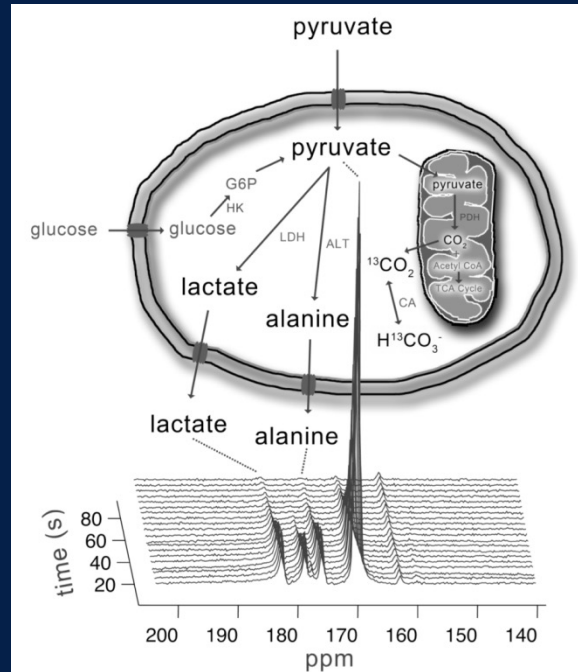
FOV: $1 / \Delta k$

Resolution: $1 / 2k_{\max}$



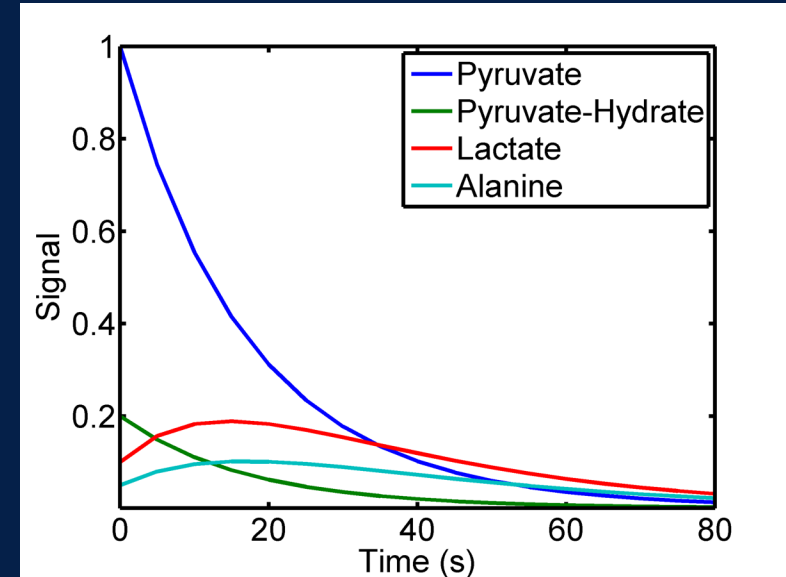
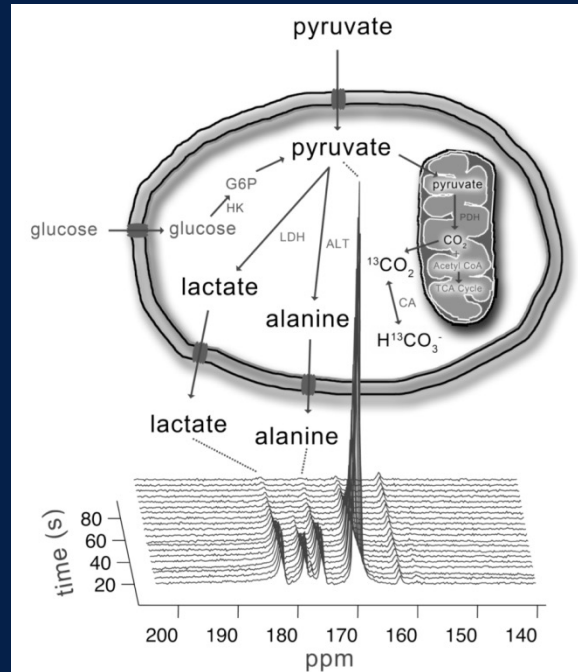
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Challenges: Metabolism & Encoding 5D Data



- Non-renewable magnetization
- Lower gyromagnetic ratio
- Metabolism + Dynamics

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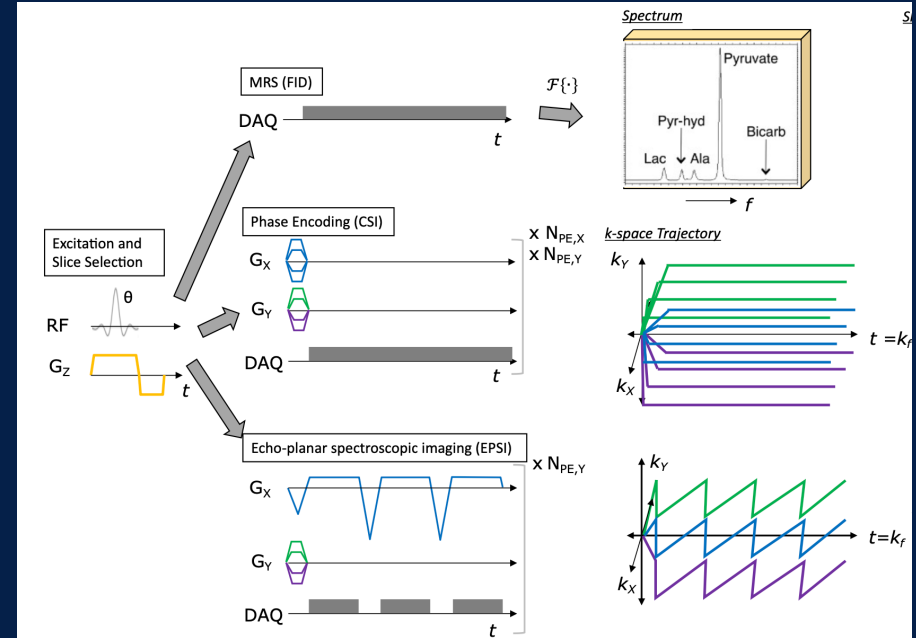


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Imaging Approaches

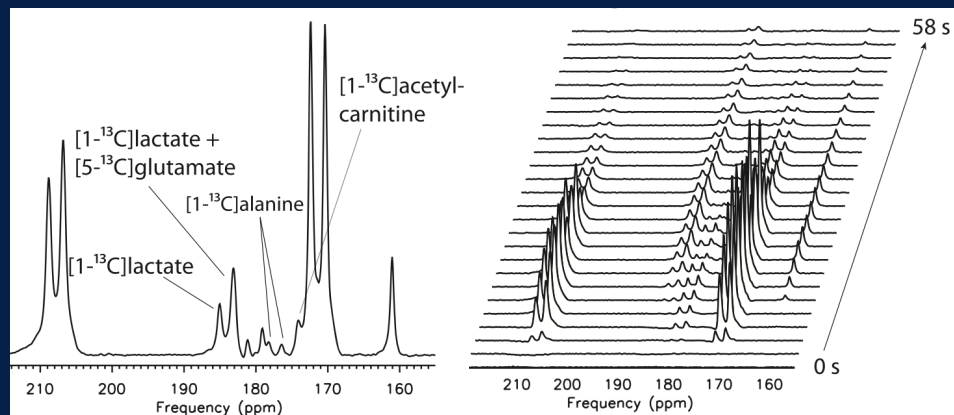
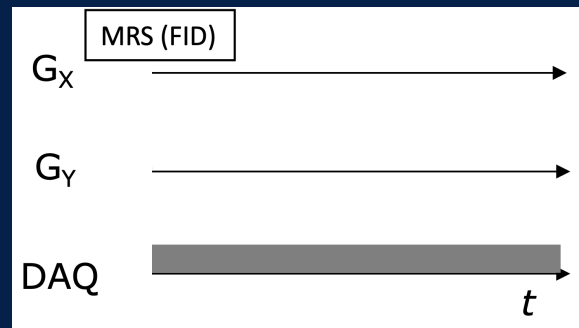
Hyperpolarized Imaging

- Three major classes of sequences:
 - Spectroscopy
 - CSI
 - Spectroscopic imaging (e.g. EPSI)
 - Model-Based Imaging (IDEAL)
 - Metabolite-Selective Imaging



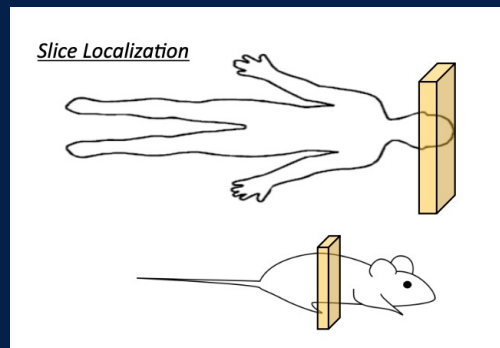
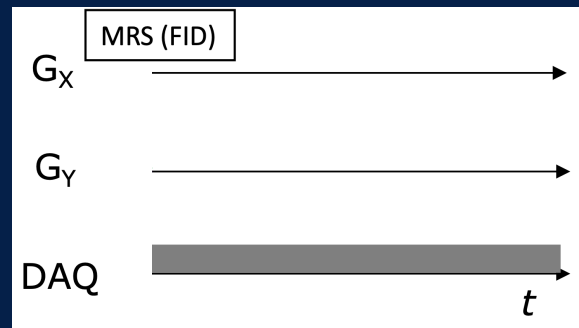
1D Dynamic MRS

- RF, no gradient
- Pros:
 - Simple & robust!
 - High spectral resolution
 - High spectral bandwidth
 - High temporal resolution



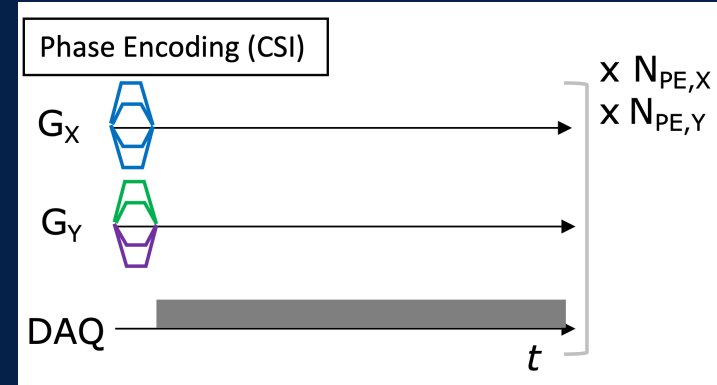
1D Dynamic MRS

- RF, no gradient
- Pros:
 - Simple & robust!
 - High spectral resolution
 - High spectral bandwidth
 - High temporal resolution
- Cons:
 - No spatial encoding!
 - Localization only from slice-select or coil profile



CSI: Chemical Shift Imaging^{1,2}

- Phase encode on both axes

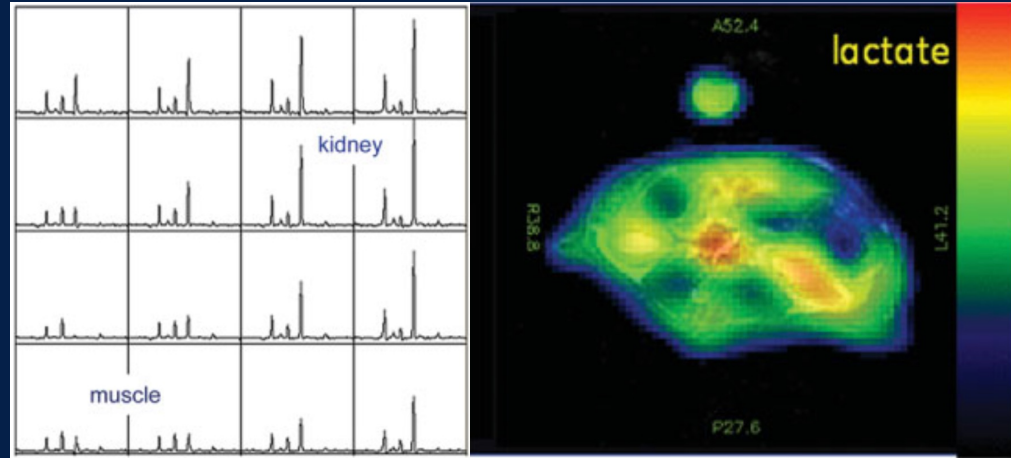


¹Kohler et al., MRM 58: 2007.

²Hurd et al., MRM 63: 2010.

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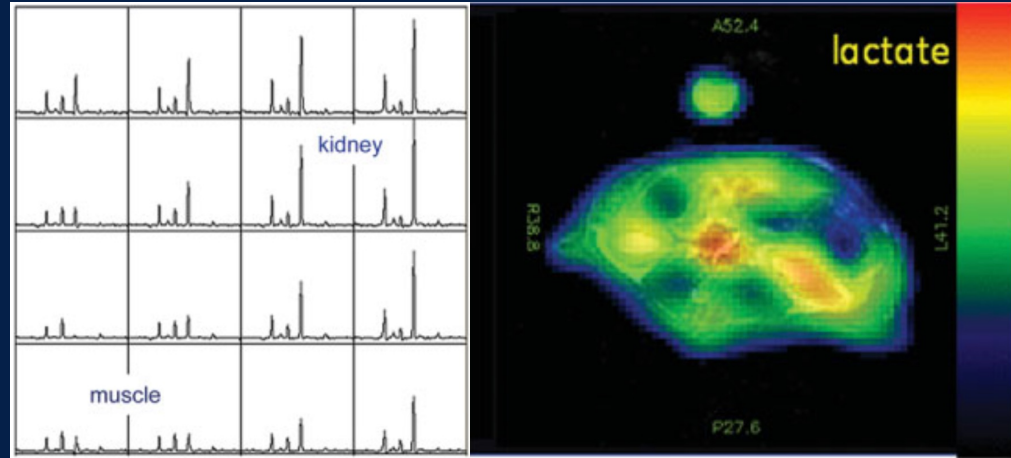


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CSI: Chemical Shift Imaging^{1,2}

- Phase encode on both axes
- Pros:
 - Spatially-resolved signal
 - High spectral resolution
 - High spectral bandwidth
- Cons:
 - S L O W
 - Scan time = $TR \times N_x \times N_y$
 - RF inefficient
 - Sensitive to motion
 - Limits volumetric coverage/dynamic imaging

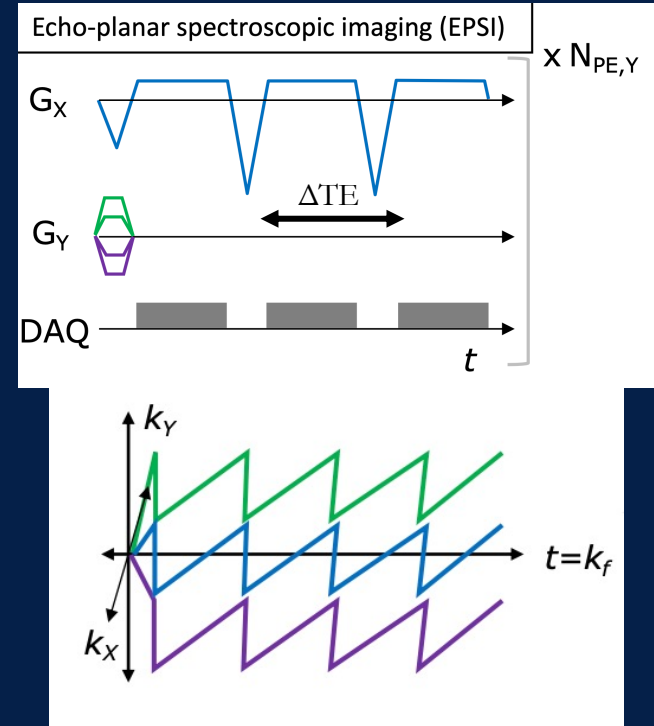


¹Kohler et al., MRM 58: 2007.

²Hurd et al., MRM 63: 2010.

MRSI: Rapid Spectroscopic Techniques

- Spiral CSI¹, EPSI², etc.
- Spectral encoding accomplished by repeating spatial gradients shifted in time by ΔTE
 - $SW = 1/\Delta TE$
 - # Echoes = 32 - 128
 - Spectral resolution = $SW/\#$ echoes
- Spatial/spectral interleaves required to fully sample k_x - k_y - k_f space



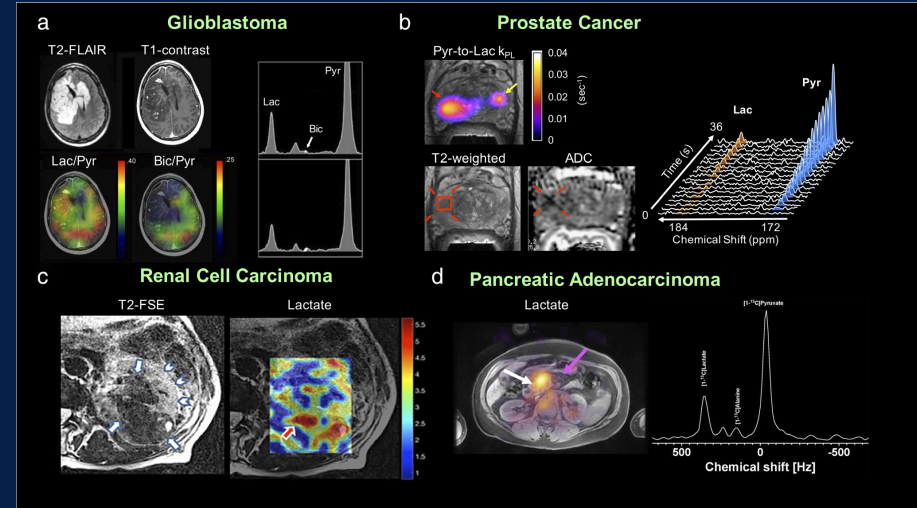
¹Mayer et al., MRM 65:2011

²Yen et al., MRM 62: 2009

MRSI: Rapid Spectroscopic Techniques

■ Pros:

- Faster than CSI
- Scan time = $TR \times N_{PE}$
- Robust, obtain a full spectrum^{1,2,3,4}



¹Park et al., MRM 2018

³Tran et al., BJR Case Rep 2019

²Chen et al., MRM 2018

⁴Stødikilde-Jørgensen et al., JMIR 2019

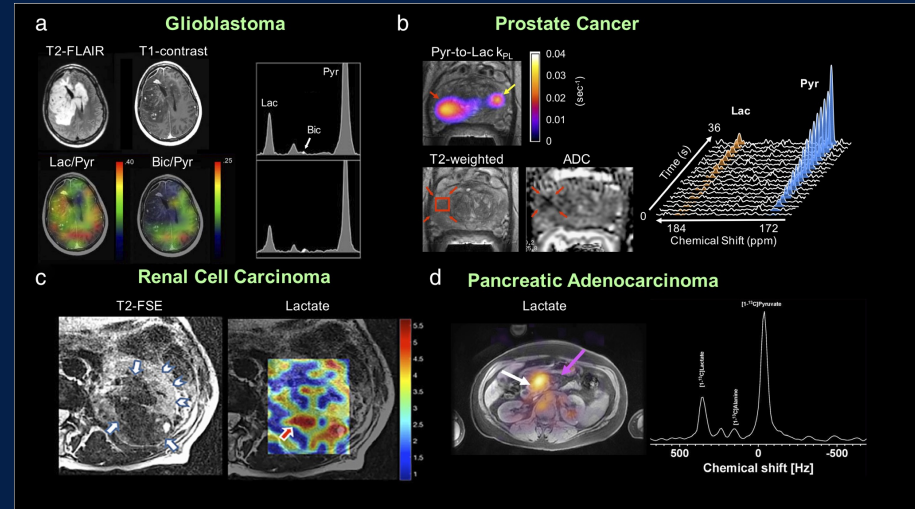
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■ Downsides:

- Sensitive to motion
- Limited spatiotemporal coverage
 - Can increase w/ compressed sensing⁵
- Lower spectral bandwidth ($1/\Delta TE$)



¹Park et al., MRM 2018

³Tran et al., BJR Case Rep 2019

⁵Larson et al., MRM 2010

²Chen et al., MRM 2018

⁴Stodkilde-Jørgensen et al., JMIR 2019

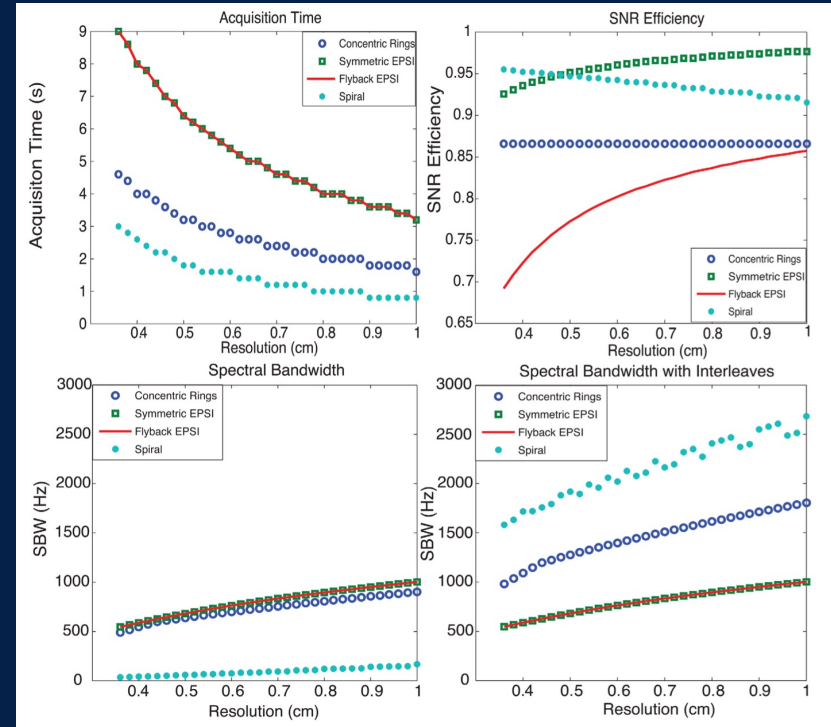
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■ Downsides:

- Sensitive to motion
- Limited spatiotemporal coverage
- Lower spectral bandwidth ($1/\Delta TE$)
- Tradeoff between spatial resolution and spectral bandwidth⁶ due to $\gamma(^{13}C)$



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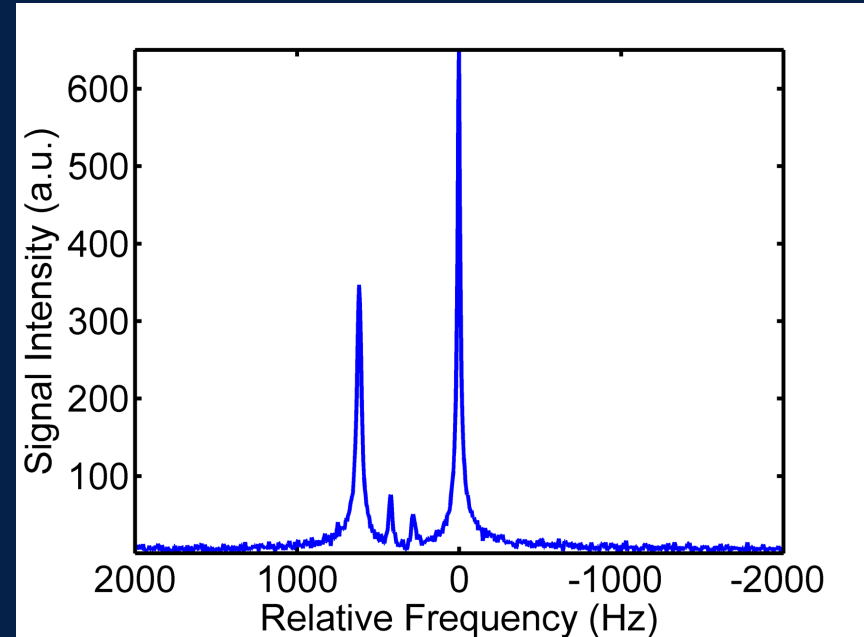
²Chen et al., MRM 2018

⁴Stodkilde-Jørgensen et al., JMRI 2019

⁶Jiang et al., MRM 75: 2016

Model-Based Imaging

- Hyperpolarized ^{13}C spectra are sparse
 - A-priori knowledge of resonances
- Can use model-based approaches (like IDEAL for fat/water) to minimize imaging requirements^{1,2}
- Use same acquisition as EPSI or spiral CSI, but:
 - No longer need to have sufficient spectral BW
 - Allow spectral aliasing, flexible choice of ΔTE
 - Arbitrary number of echoes ($\# \text{ echoes} > \# \text{ freq} + 1$)



¹Reeder et al., JMRI 26: 2007

²Wiesinger et al., MRM 68(1): 2012

Model-Based Imaging: How to choose ΔTE

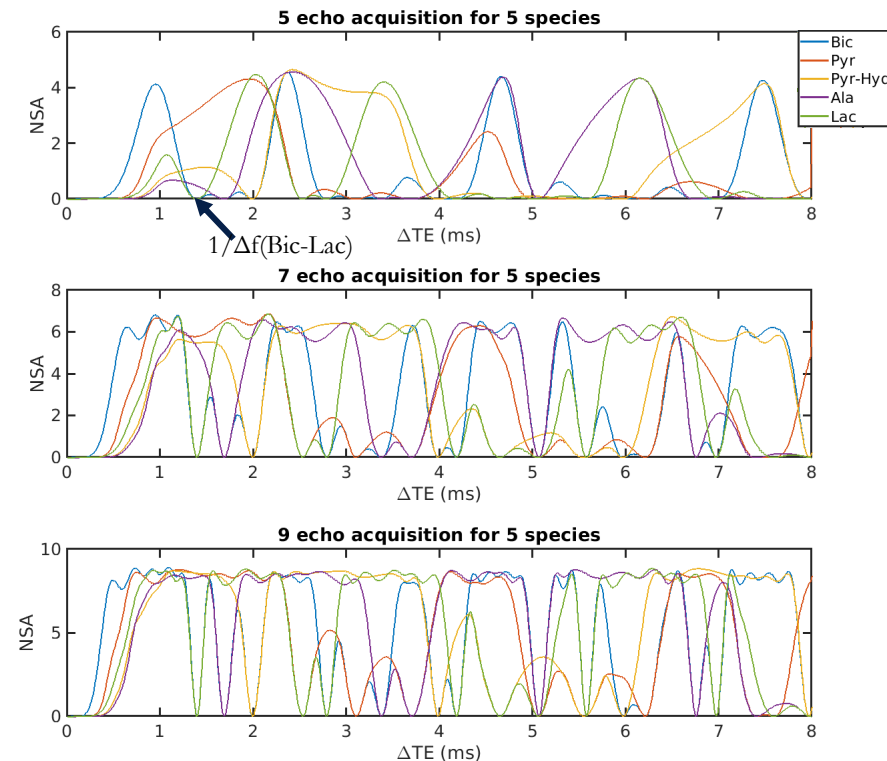
■ How to choose echo spacing (ΔTE)?

- Intuitively want unique phase at each echo
 - $\Delta TE = 1/\Delta f \rightarrow$ overlapping peaks, can't resolve
- How to choose with multiple frequencies?
- Calculate # of signal averages (NSA) as a function of echo-spacing and # echoes

$$NSA_i = \frac{1}{\text{diag}_i((A^H A)^{-1})}$$

$$A_n^i = \exp(i2\pi\Delta f_i TE_n)$$

- Optimally, NSA = # echoes and will decrease when there is insufficient phase accrual



Signal Model

- IDEAL can be applied in image-space or k-space
- Image space¹:

$$S(\text{TE}_n) = \left(\sum_{i=1}^N \rho_i e^{2\pi i \Delta f_i \text{TE}_n} \right) e^{2\pi i \psi \text{TE}_n}$$

- k-space^{2,3,4}:

$$\hat{s}_n(\tau_{k,n}, \mathbf{k}) = \sum_{m=1}^M \rho_m(\mathbf{k}) e^{i2\pi \Delta f_m(t_n + \tau_{k,n})},$$

Signal at k-space point $\mathbf{k}$
sampled at echo n

Unknown spin
density

Known phase from
chemical shift

- With a known field map, this becomes a linear problem
- Solve for ρ_m with a least-squares approach point-by-point in image- or k- space

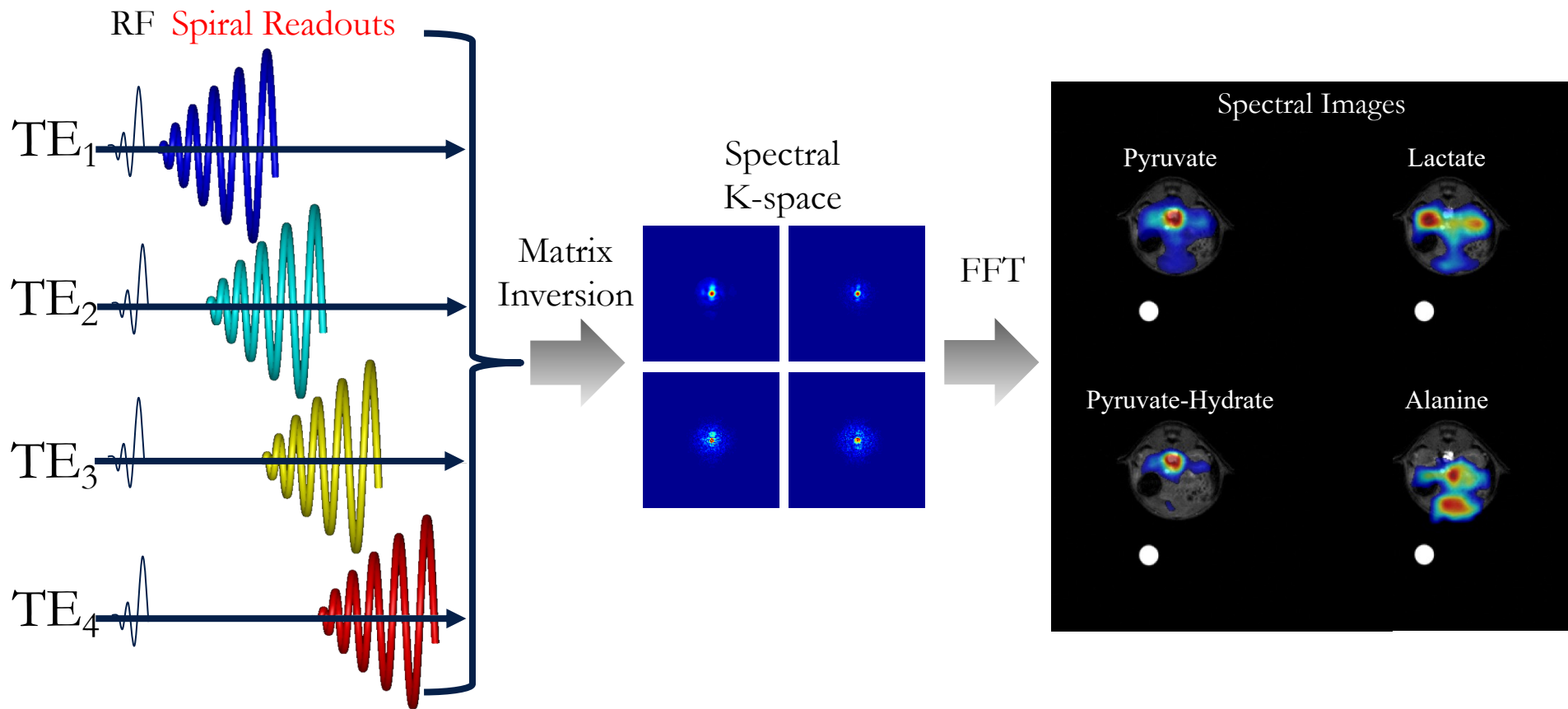
¹Reeder et al., MRM 2007

³Brodsky et al., MRM 59: 2008

²Traechtler et al., MRM 2021

⁴Wiesinger et al., MRM 68(1): 2012

Model-Based Reconstruction



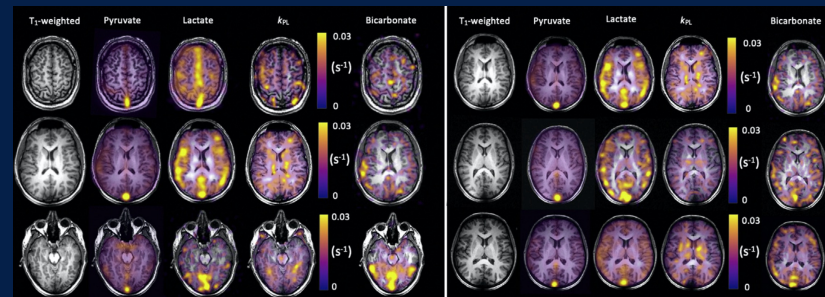
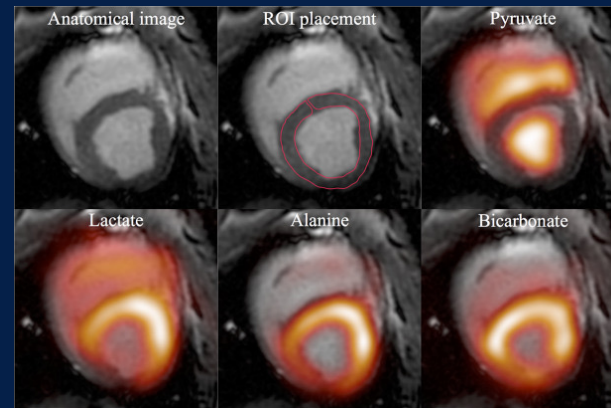
¹Brodsky et al. MRM 59(5): 2008

²Wiesinger et al., MRM 68(1): 2012

Model-Based Imaging

■ Pros:

- Faster than 'standard' MRSI
 - Single-shot scan time = $TR \times N_{\text{echoes}}$
- Better spatiotemporal coverage^{1,2}



¹Tougaard et al., MRM 2018

³Wiens et al., MRM 2014

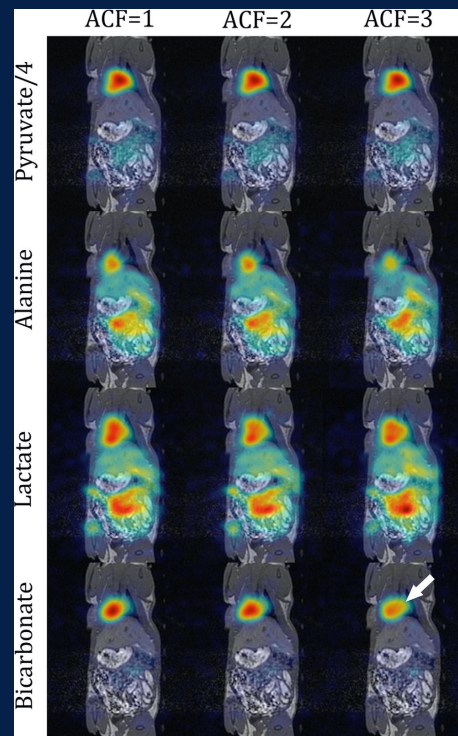
²Grist et al., Neuroimage 2019

⁴Reeder et al., MRM 2007

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- Can incorporate field map, parallel imaging, compressing sensing into reconstruction³



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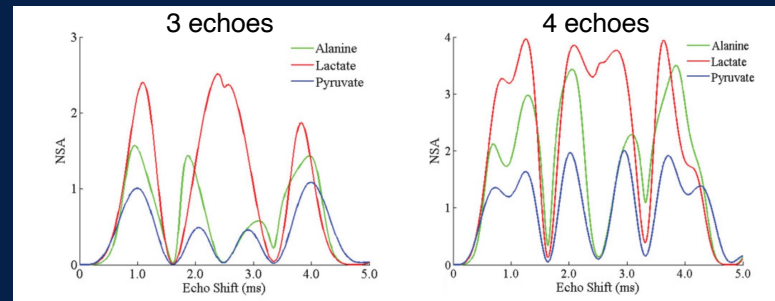
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■ Challenges:

- ΔTE needs to be carefully chosen⁴
- Requires prior knowledge and accurate model of the spectrum
- # echoes can be prohibitive for complicated spectra



¹Tougaard et al., MRM 2018

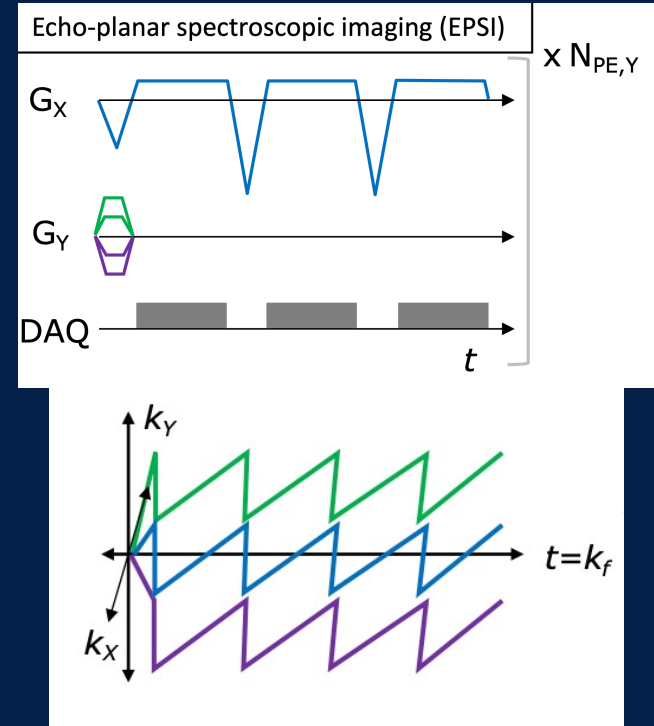
³Wiens et al., MRM 2014

²Grist et al., Neuroimage 2019

⁴Reeder et al., MRM 2007

Metabolite-Specific Imaging

- CSI and MRSI jointly encode spatial and spectral data



¹Gordon et al., MRM 2018

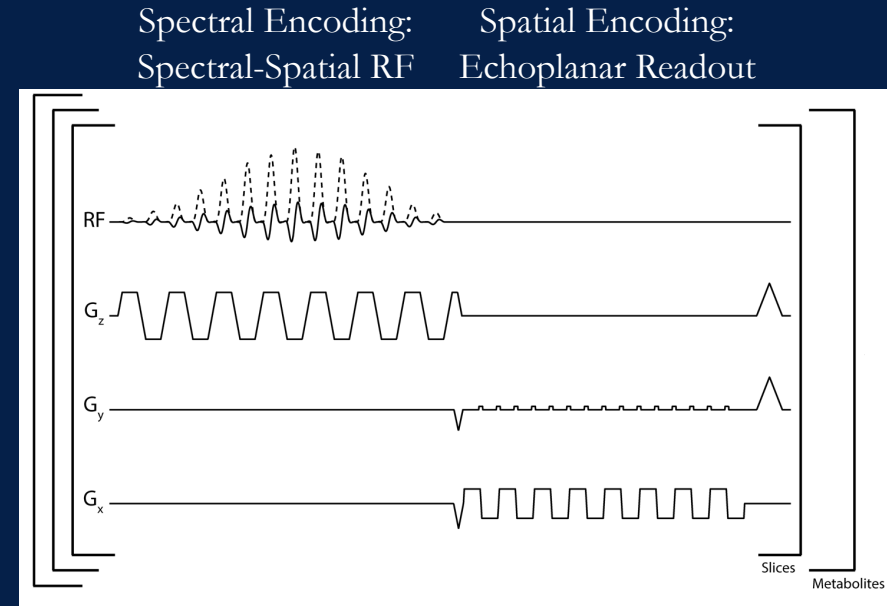
³Cunningham et al., Circ Res 2016

²Lee et al., Neuroimage 2020

⁴Ma et al., MRM 2022

Metabolite-Specific Imaging

- CSI and MRSI jointly encode spatial and spectral data
- Metabolite-selective imaging separates encoding into two separate steps
 - RF pulse: Spectral encoding
 - Imaging readout: Spatial encoding
- Without the need for spectral encoding, can employ fast, single-shot readouts
 - EPI^{1,2}
 - Spiral^{3,4}



¹Gordon et al., MRM 2018

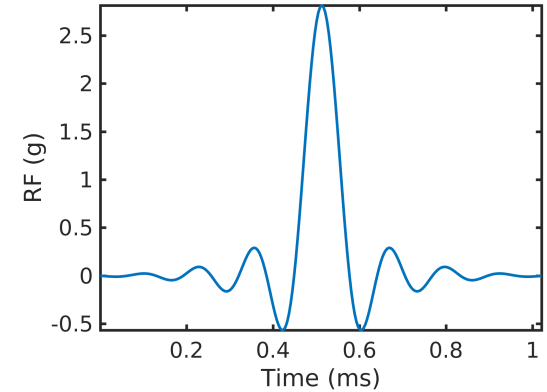
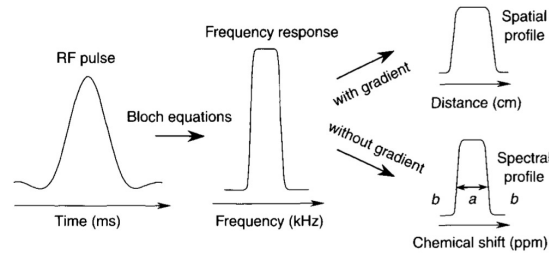
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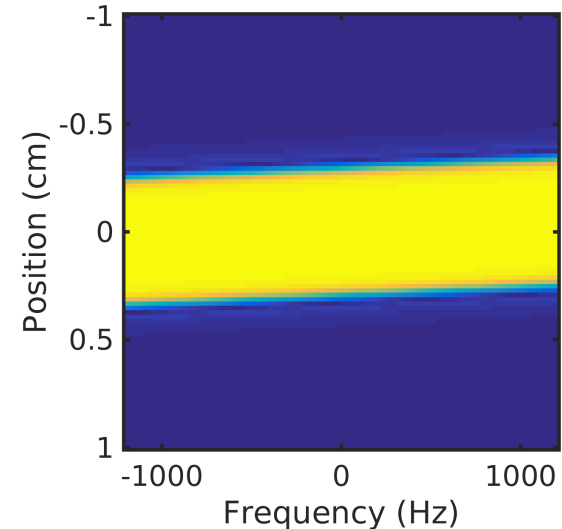
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Slice-Selective Excitation

Conventional RF pulses (i.e. sinc) can only be either spatially or spectrally selective

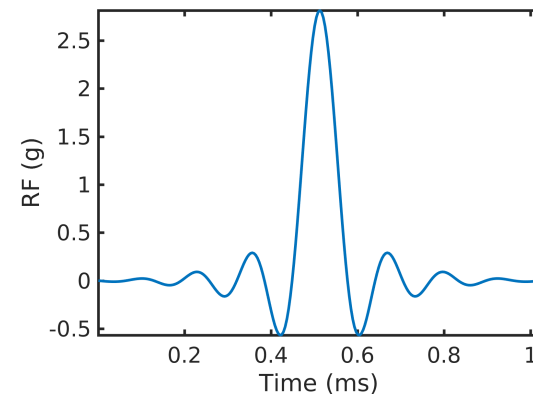
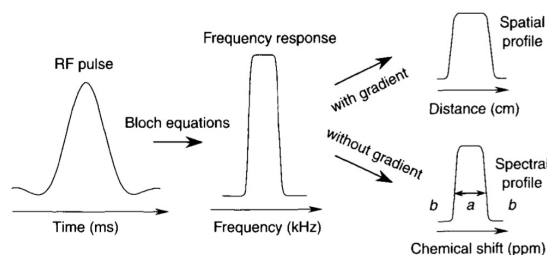


- When multiple resonances are present:
 - Not frequency selective
 - Chemical shift displacement artifact in the slice dimension

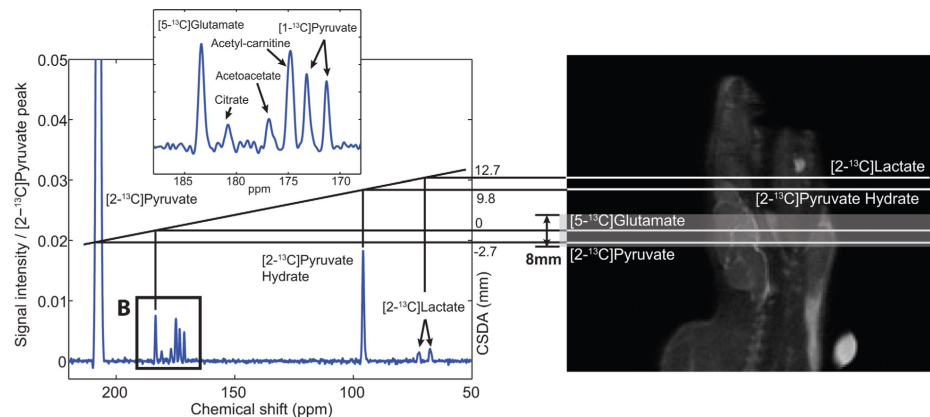


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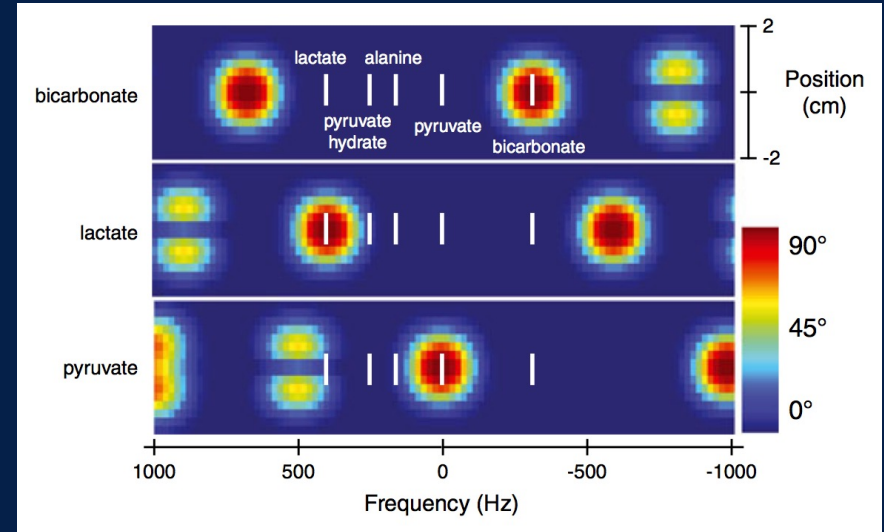
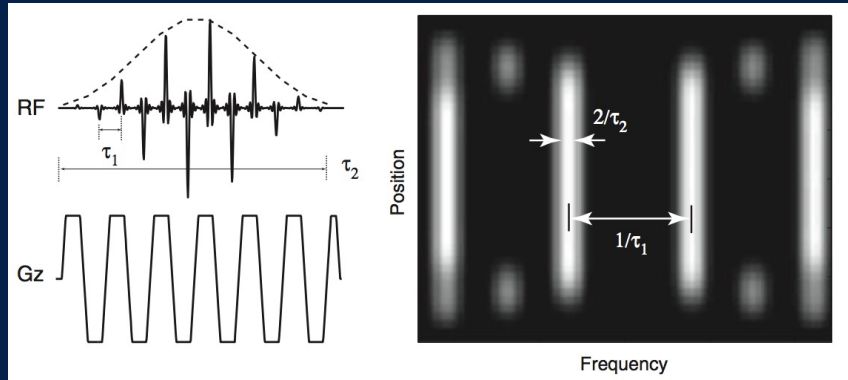
Conventional RF pulses (i.e. sinc) can only be either spatially or spectrally selective



- When multiple resonances are present:
 - Not frequency selective
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Spectral-Spatial RF Pulses^{1,2,3}



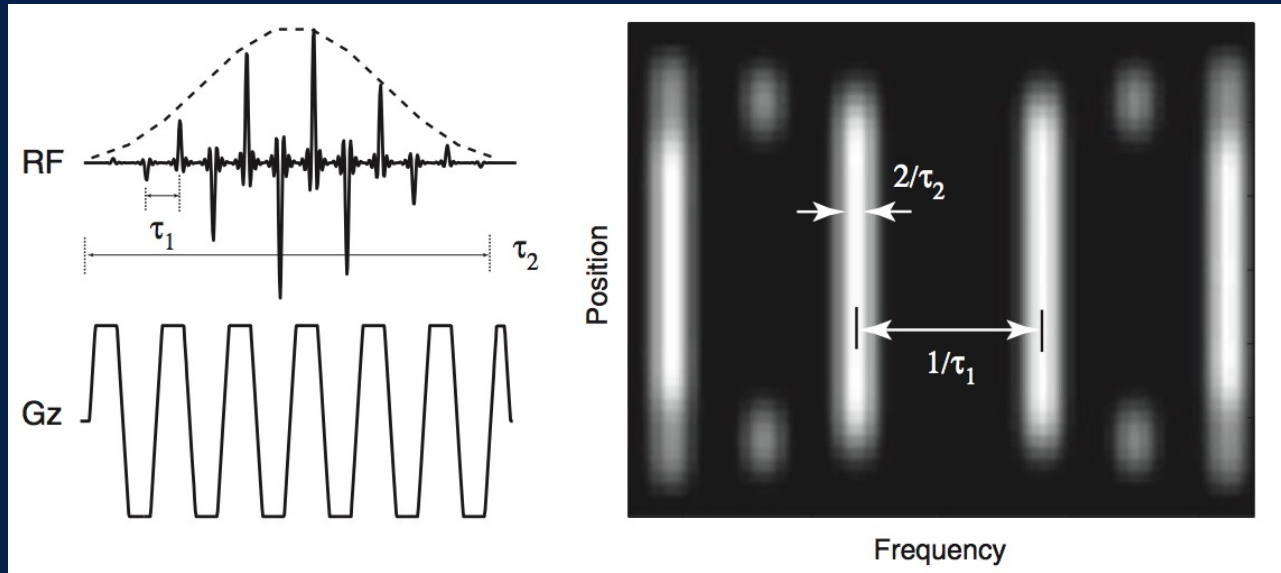
- Spectral-spatial pulses are selective in both frequency and space
- Add oscillating gradient for additional spatial selectivity
 - Subpulses control spatial selectivity
 - # of subpulses and their separation control spectral selectivity

¹Lau et al., NMR in Biomedicine 2011

²Larson et al., JMR 2008

³Kerr et al., ISMRM 2008: #226

Spectral-Spatial RF Pulses^{1,2,3}



General guidelines:

1. Passband FWHM is inversely proportional to SPSP RF pulse duration (Long pulses)
2. Stopband width inversely proportional to subpulse spacing (Spectral/spatial tradeoff)
3. Spatial (slice profile) is approximately the FT of an individual subpulse (Limited thickness)

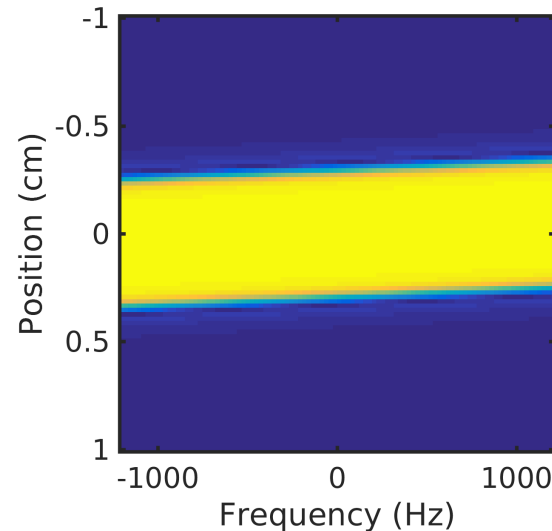
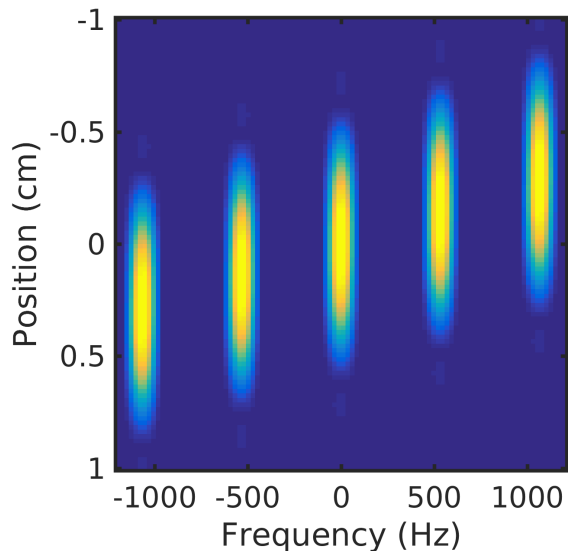
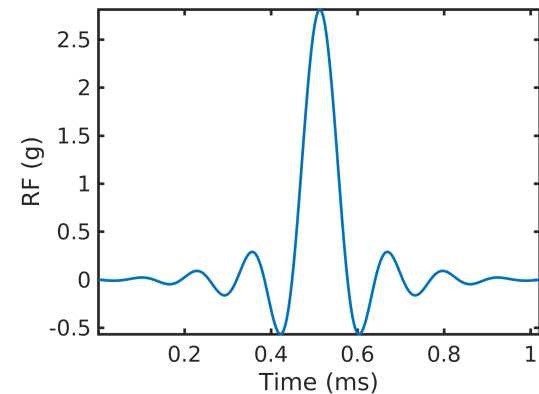
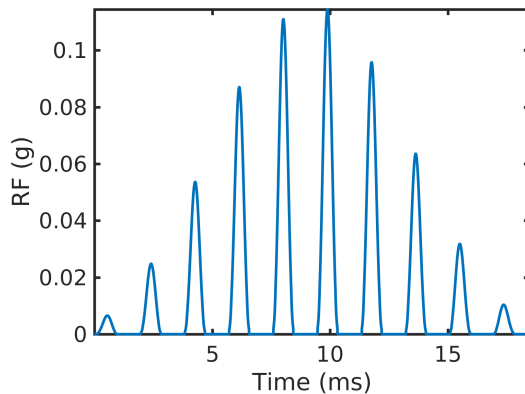
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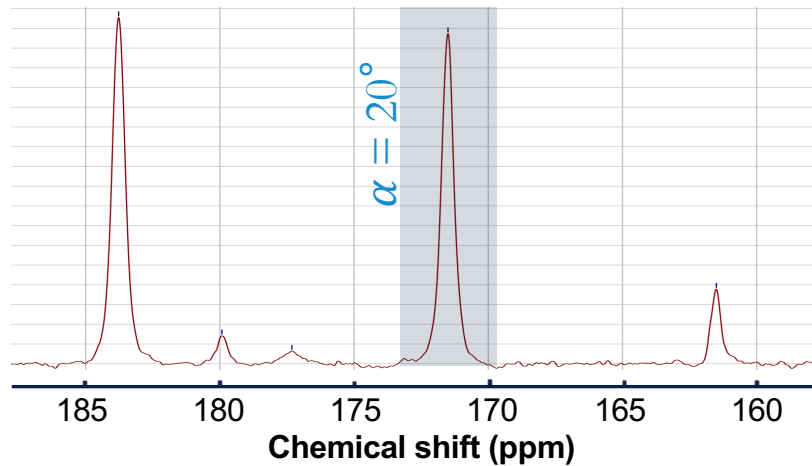
³Kerr et al., ISMRM 2008: #226

Spectral-Spatial Excitation

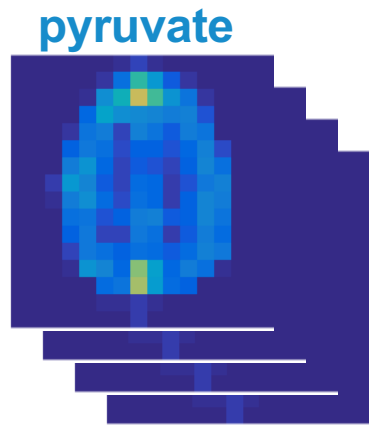
- Slice *AND* frequency selective
- No chemical shift displacement artifact
- Easy to use variable flip angle scheme



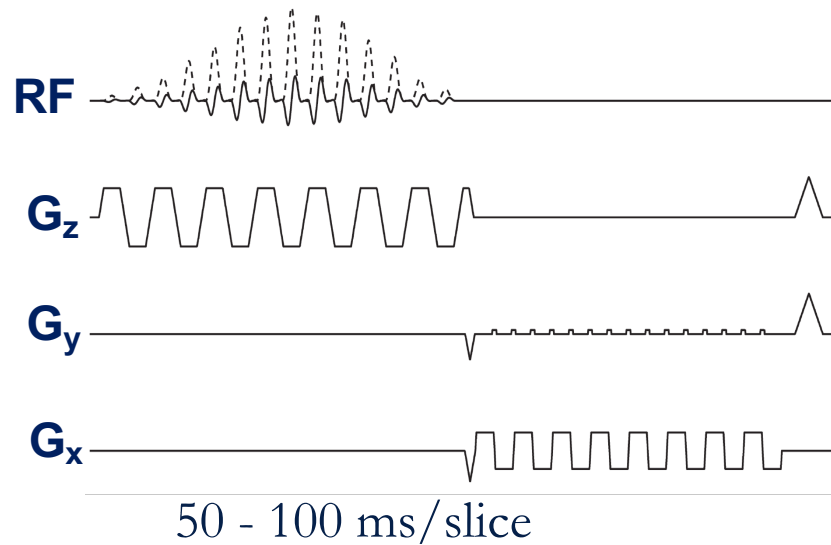
^{13}C spectra



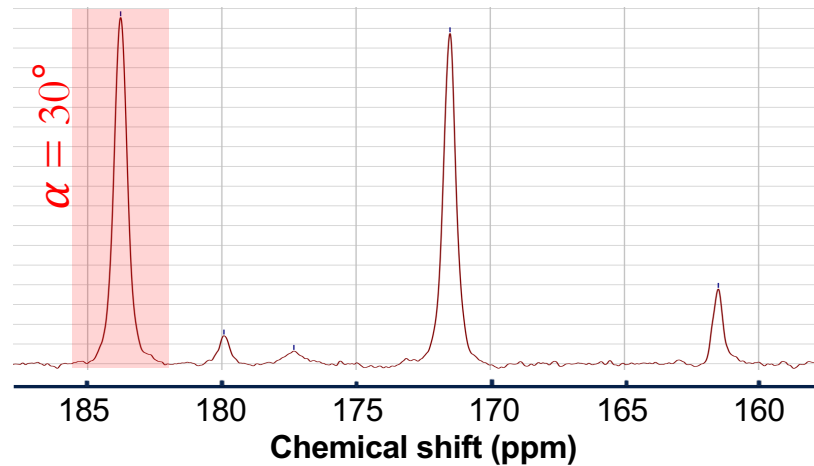
HP- ^{13}C EPI



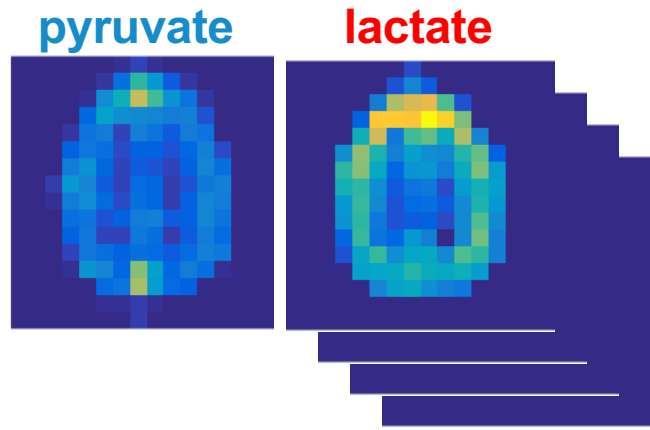
SPSP excitation



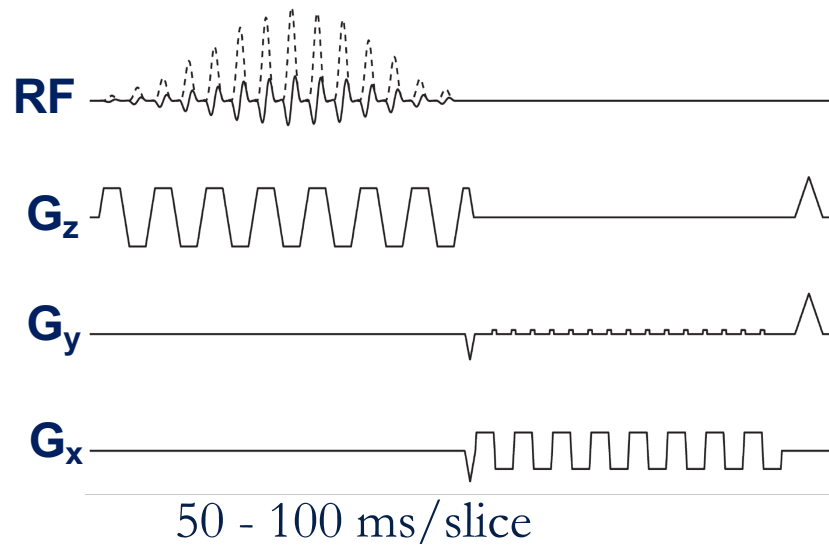
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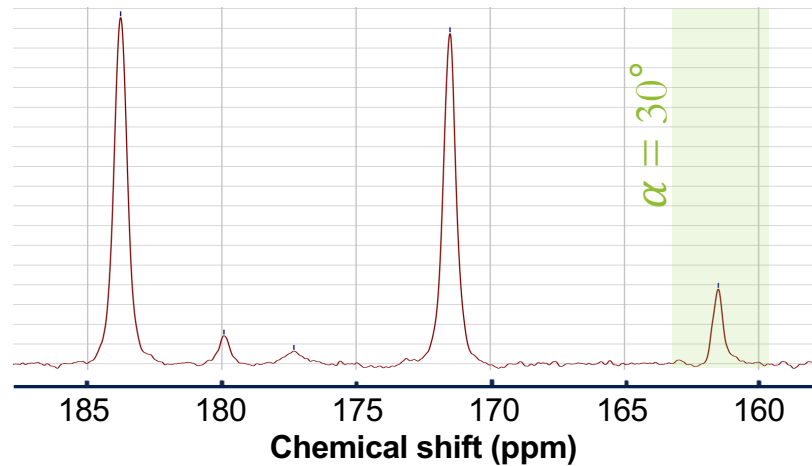
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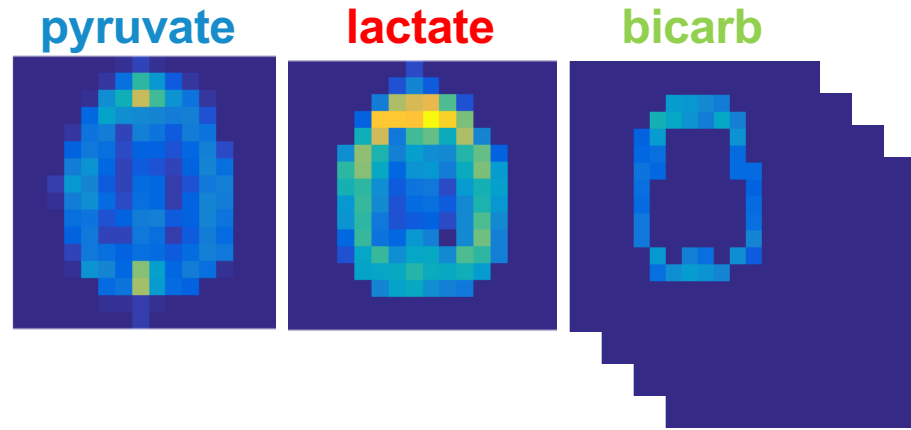
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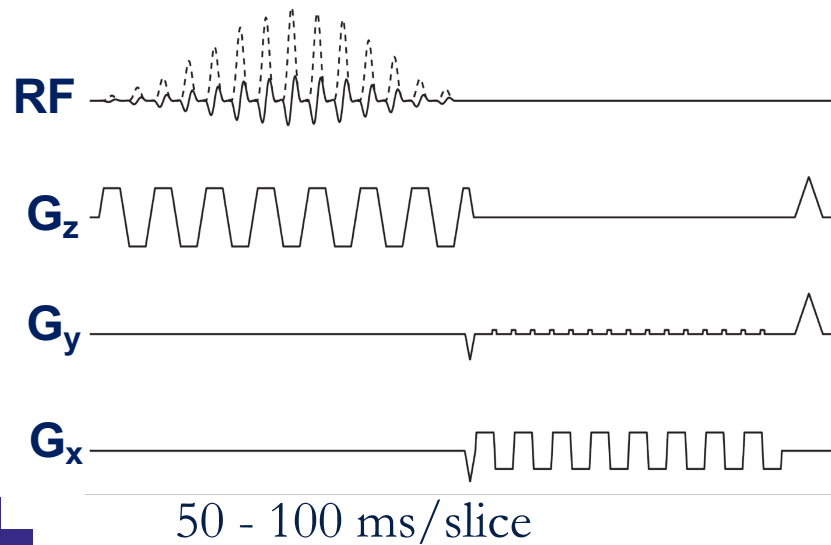
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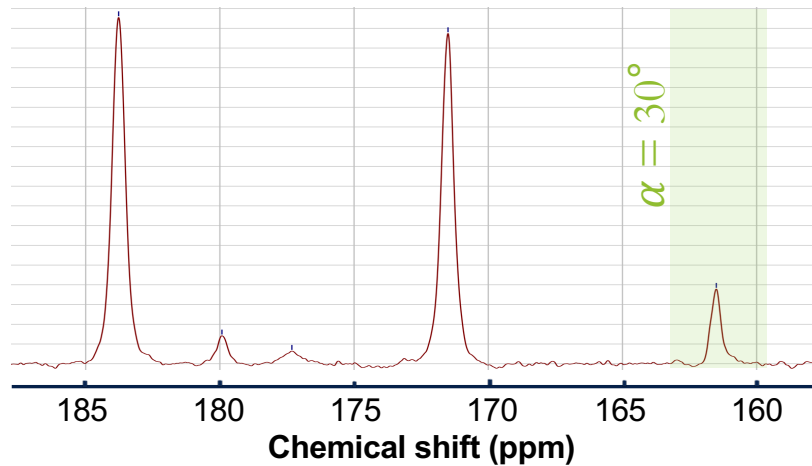
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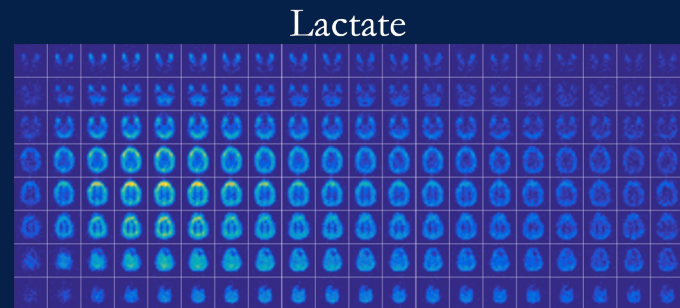
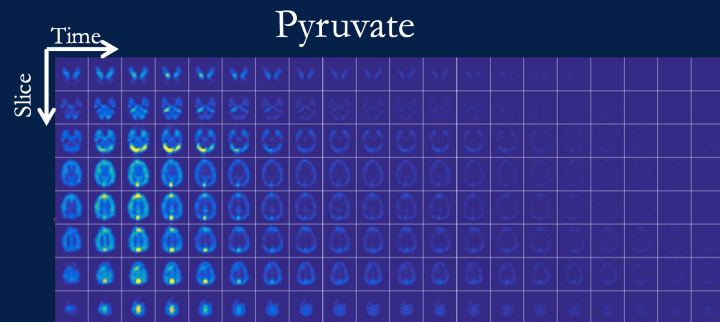
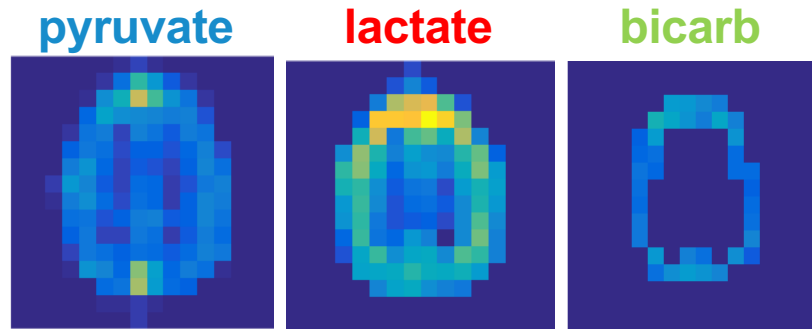
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^{13}C spectra



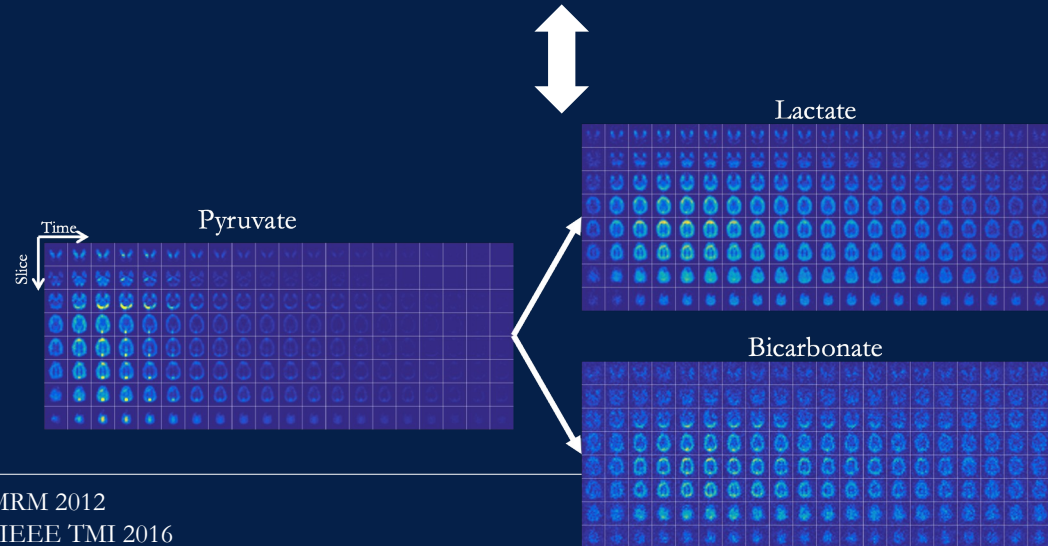
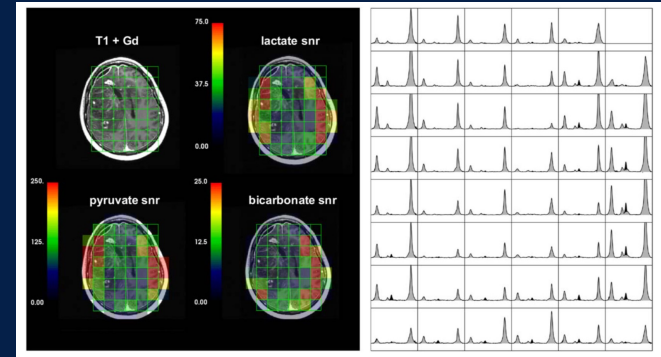
HP- ^{13}C EPI



Metabolite-Specific Imaging

■ Pros

- Fast!
 - Scan time = $TR \times \# \text{ slices} \times \# \text{ metabolites}$
 - $\uparrow$ volumetric coverage
- Robust to motion
- Easily extendable to large FOVs



¹Wespi et al., NMR in Biomed 2018

³Lau et al., MRM 2018

⁵Schulte et al., MRM 2012

²Geraghty et al., MRM 2016

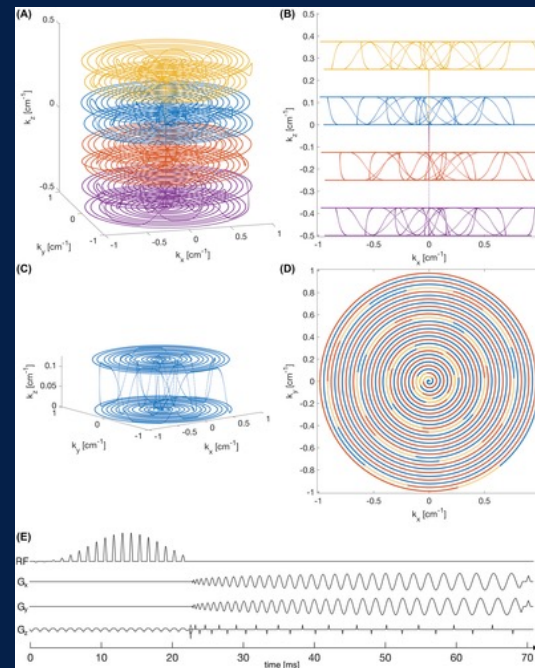
⁴Olin et al., MRM 2020

⁶Maidens et al., IEEE TMI 2016

Metabolite-Specific Imaging

■ Pros

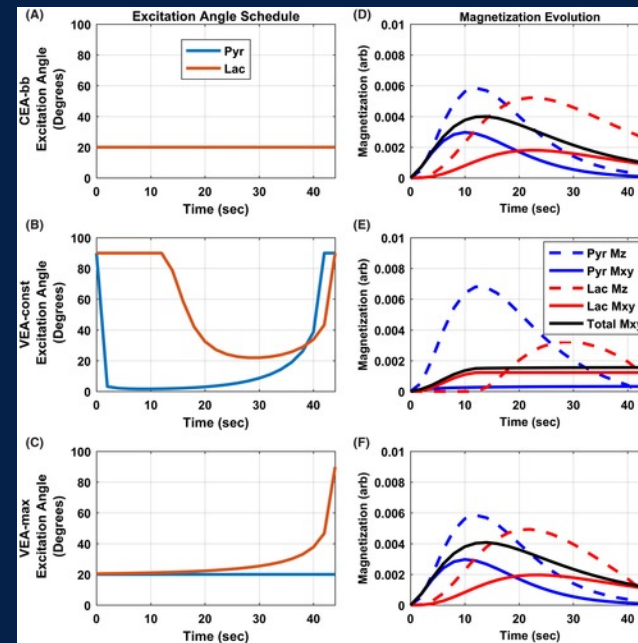
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 - Scan time = $TR \times \# \text{ slices} \times \# \text{ metabolites}$
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- Readily incorporate extra features:
 - Compressed sensing^{1,2}



Metabolite-Specific Imaging

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 - Scan time = $TR \times \# \text{ slices} \times \# \text{ metabolites}$
 - $\uparrow$ volumetric coverage
- Robust to motion
- Easily extendable to large FOVs
- Readily incorporate extra features:
 - Compressed sensing^{1,2}
 - Parallel imaging^{3,4}
 - Independent flip angles^{5,6}
 - Variable resolution



¹Wespi et al., NMR in Biomed 2018

³Lau et al., MRM 2018

⁵Schulte et al., MRM 2012

²Geraghty et al., MRM 2016

⁴Olin et al., MRM 2020

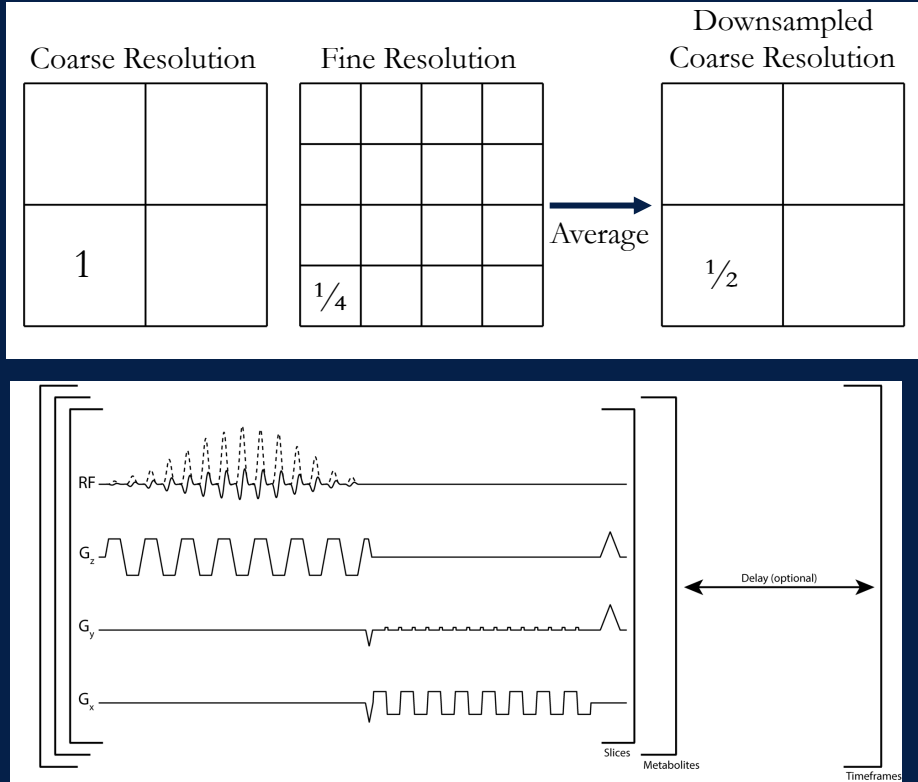
⁶Maidens et al., IEEE TMI 2016

Sequence Options

- SNR in MRI is proportional to voxel volume¹

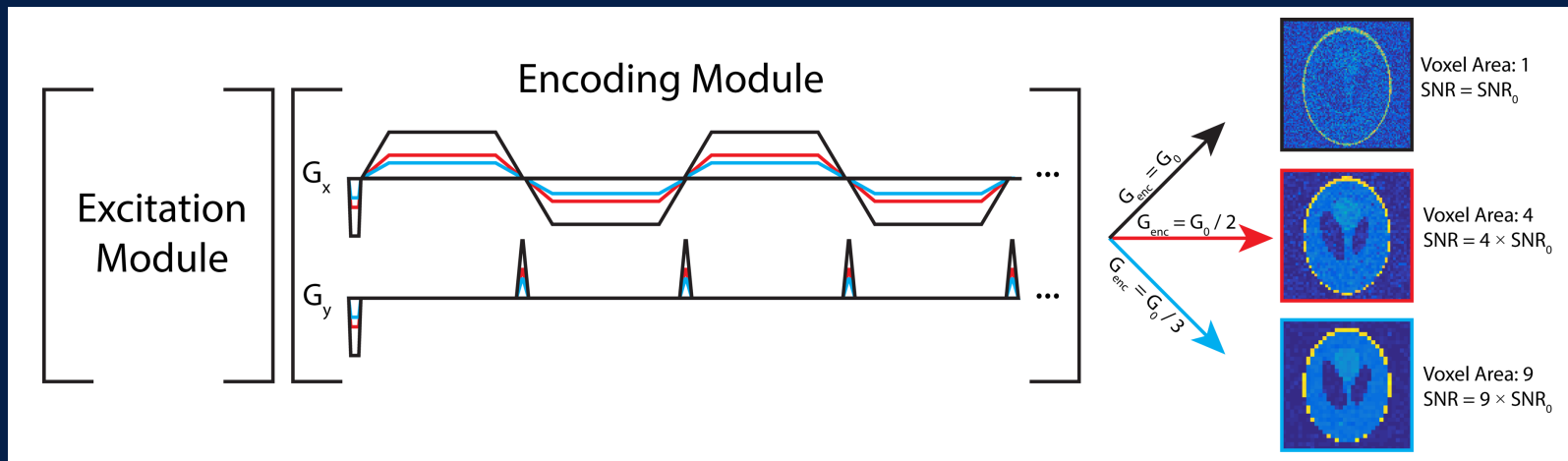
$$SNR = \frac{\Delta x \Delta y \Delta z \sqrt{NEX}}{\sqrt{BW}}$$

- Downsampling only improves SNR by $\sqrt{\text{voxel volume}}$
- Spectroscopic imaging (EPSI/CSI) encodes spatial + spectral dimensions simultaneously can't exploit this
- But metabolite-selective imaging sequences can!



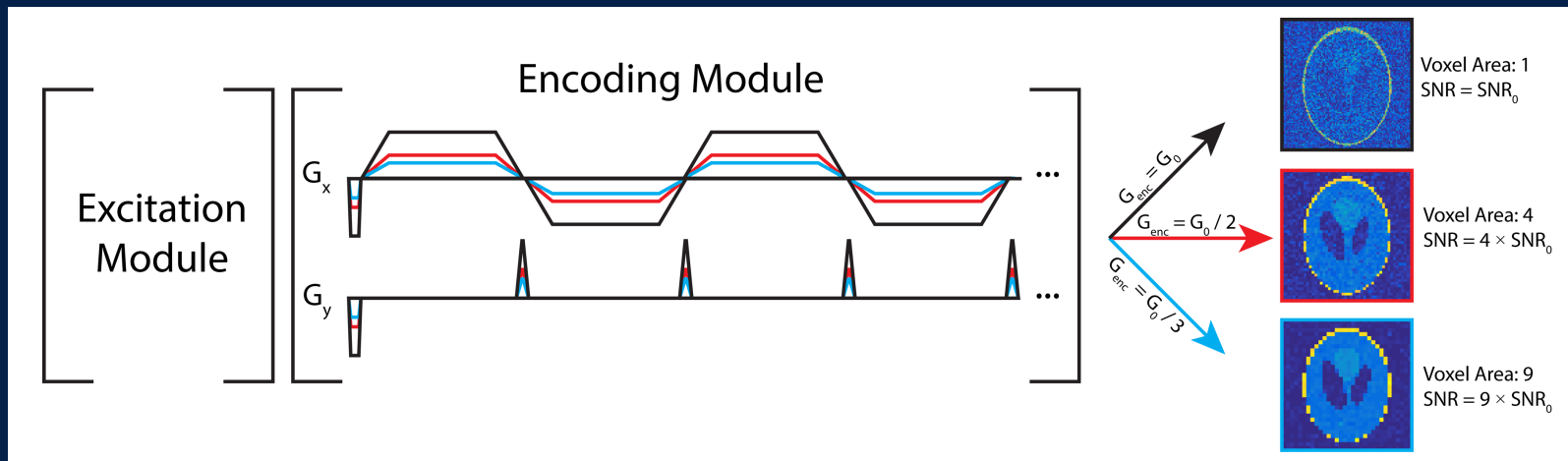
¹Edelstein et al., MRM 1986.

Variable-Resolution Imaging¹



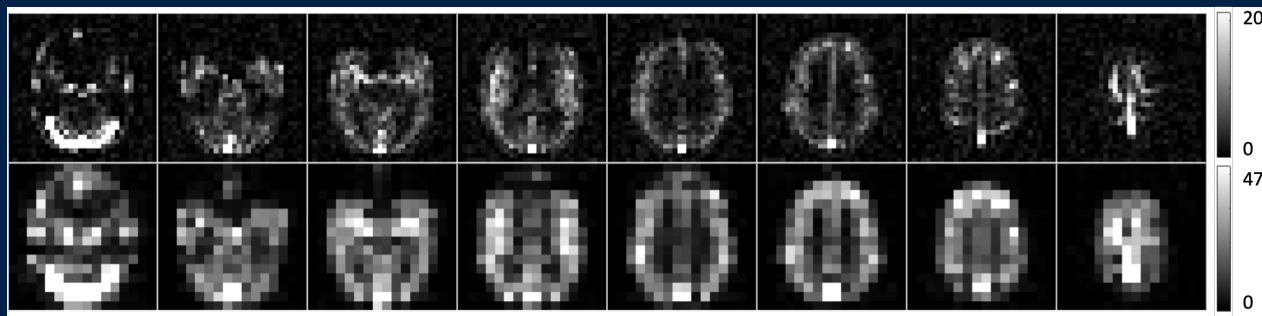
- Eliminates the tradeoff in SNR/spatial resolution for pyruvate and metabolites
 - High-resolution for pyruvate and coarser resolution for metabolites
- Improved SNR over voxel-averaging after acquisition

Variable-Resolution Imaging¹



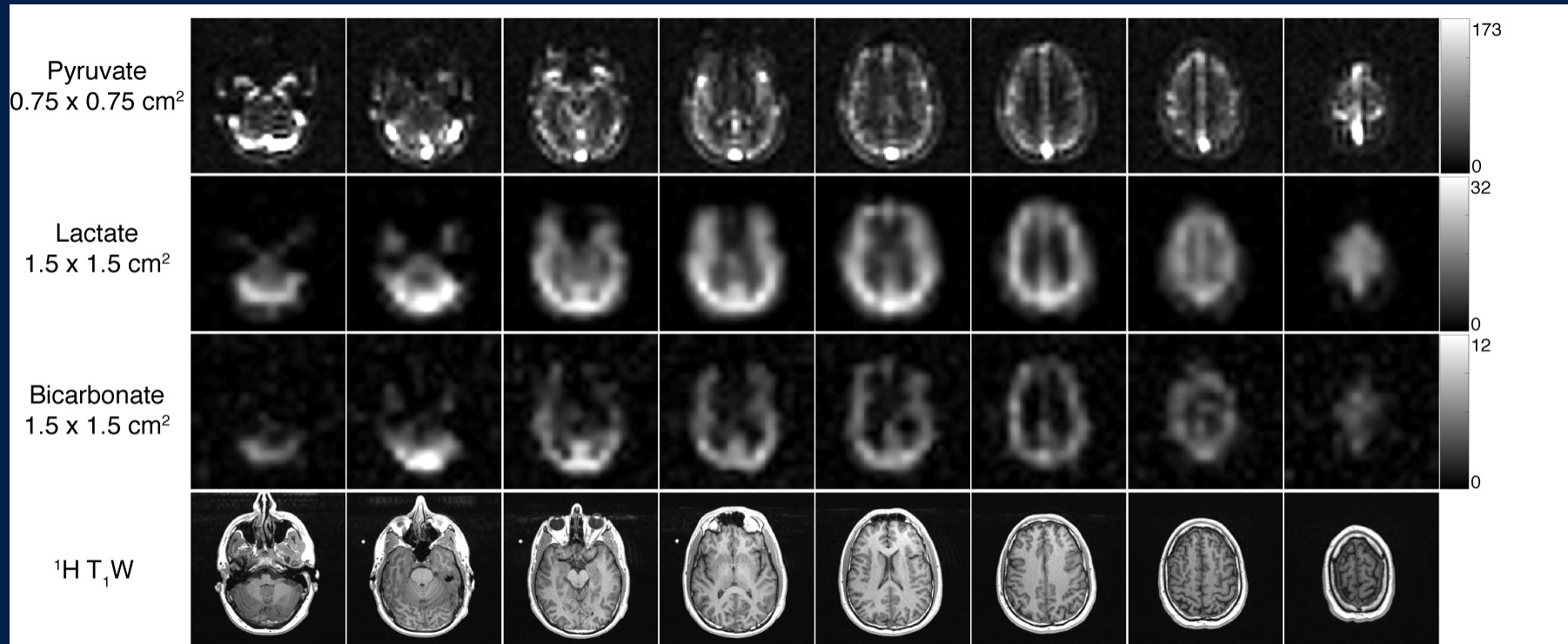
Pyruvate
 $7.5 \times 7.5 \text{ mm}^2$

Pyruvate
 $15 \times 15 \text{ mm}^2$



¹Gordon et al., MRM 2020

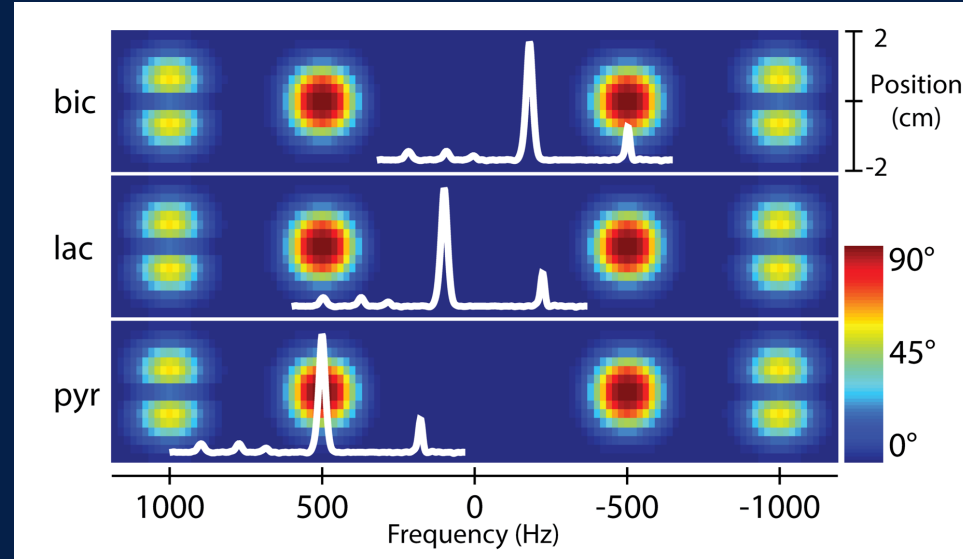
Healthy Human Volunteer: Brain AUC



Metabolite-Specific Imaging

■ Challenges:

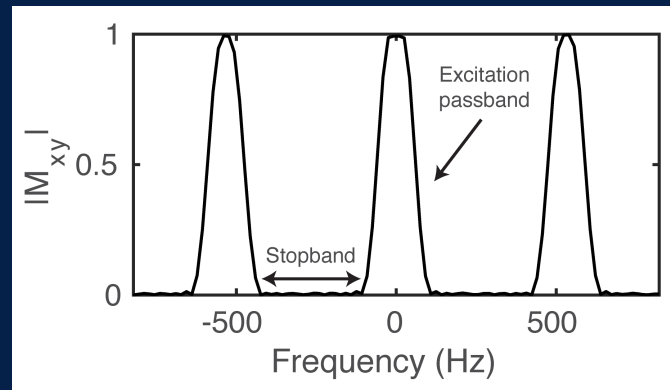
- Need sparse, well-resolved spectrum¹
 - Passband FWHM inversely proportional to SPSP duration
 - Typically want >90 Hz separation between metabolites
- Long RF pulses (15-20ms)
 - Not suitable for short T2*



Metabolite-Specific Imaging

■ Challenges:

- Need sparse, well-resolved spectrum¹
- Long RF pulses (15-20ms)
- Sensitive to off-resonance
 - Reduced flip angle



¹Lau et al., NMR in Biomed 2011

³Lee et al., MRM 2022

⁵Miller et al., MRM 2018

²Grist et al., MRM 2020

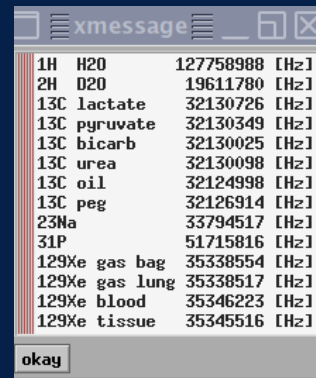
⁴Lau et al., MRM 2010

⁶Geraghty et al., MRM 2018

Metabolite-Specific Imaging

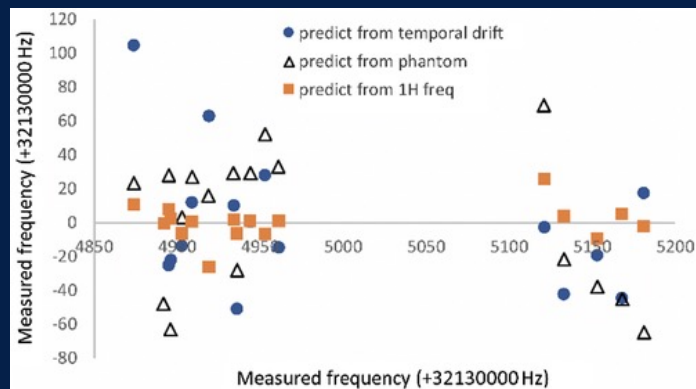
Challenges:

- Need sparse, well-resolved spectrum¹
- Long RF pulses (15-20ms)
- Sensitive to off-resonance
 - Reduced flip angle
 - Center-frequency calibration using urea or water reference²



1H	H2O	127758988	[Hz]
2H	D2O	19611780	[Hz]
13C	lactate	32130726	[Hz]
13C	pyruvate	32130349	[Hz]
13C	bicarb	32130025	[Hz]
13C	urea	32130098	[Hz]
13C	oil	32124998	[Hz]
13C	peg	32126914	[Hz]
23Na		33794517	[Hz]
31P		51715816	[Hz]
129Xe	gas bag	35338554	[Hz]
129Xe	gas lung	35338517	[Hz]
129Xe	blood	35346223	[Hz]
129Xe	tissue	35345516	[Hz]

okay



¹Lau et al., NMR in Biomed 2011

³Lee et al., MRM 2022

⁵Miller et al., MRM 2018

²Grist et al., MRM 2020

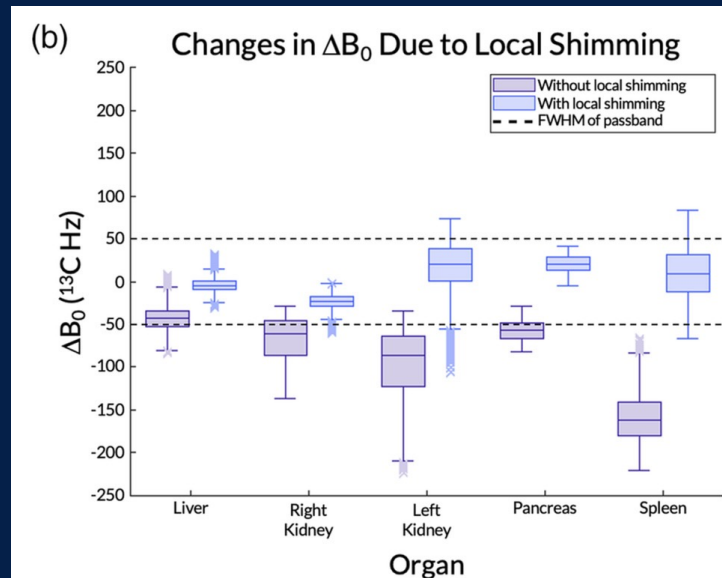
⁴Lau et al., MRM 2010

⁶Geraghty et al., MRM 2018

Metabolite-Specific Imaging

■ Challenges:

- Need sparse, well-resolved spectrum¹
- Long RF pulses (15-20ms)
- Sensitive to off-resonance
 - Reduced flip angle
 - Center-frequency calibration using urea or water reference²
 - Blurring/distortion
 - Shimming can provide <1 ppm ΔB_0 under most conditions³



¹Lau et al., NMR in Biomed 2011

³Lee et al., MRM 2022

⁵Miller et al., MRM 2018

²Grist et al., MRM 2020

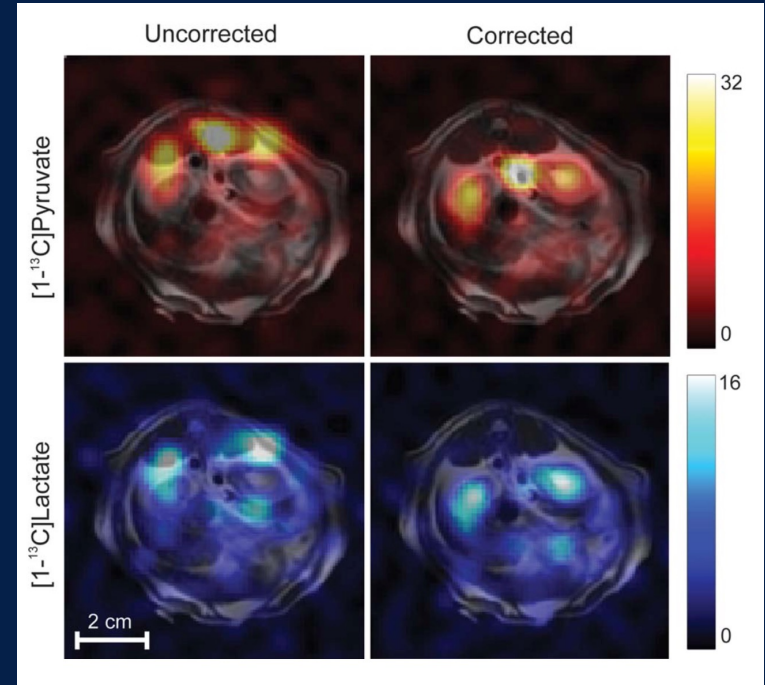
⁴Lau et al., MRM 2010

⁶Geraghty et al., MRM 2018

Metabolite-Specific Imaging

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- Long RF pulses (15-20ms)
- Sensitive to off-resonance
 - Reduced flip angle
 - Center-frequency calibration using urea or water reference²
 - Blurring/distortion
 - Shimming can provide <1 ppm ΔB_0 under most conditions³
 - Can incorporate ^1H methods to remove distortion/blurring^{4,5,6}



¹Lau et al., NMR in Biomed 2011

³Lee et al., MRM 2022

⁵Miller et al., MRM 2018

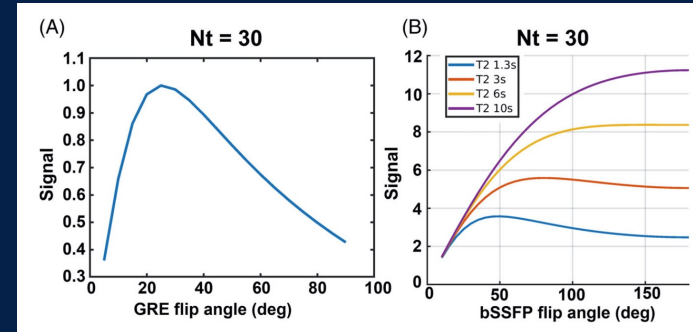
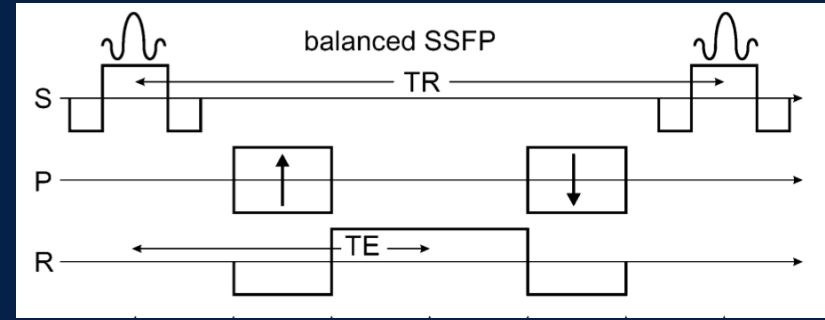
²Grist et al., MRM 2020

⁴Lau et al., MRM 2010

⁶Geraghty et al., MRM 2018

bSSFP Imaging

- All prior sequences were GRE (no refocusing)
- Refocused approaches, like bSSFP, can be used
 - Net gradient area is zero
 - RF alternates 180°
- In principle, offers highest SNR efficiency

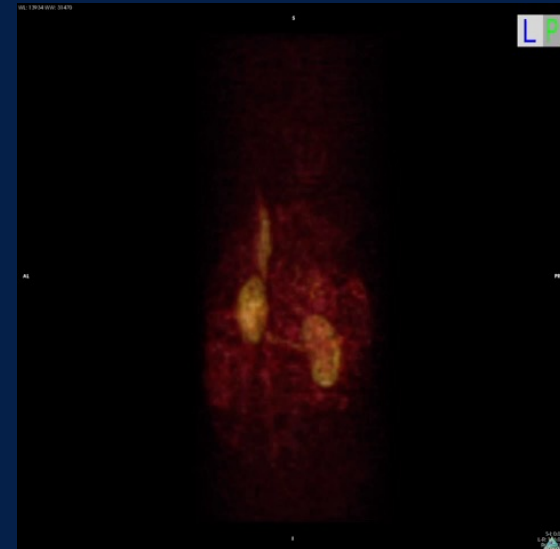
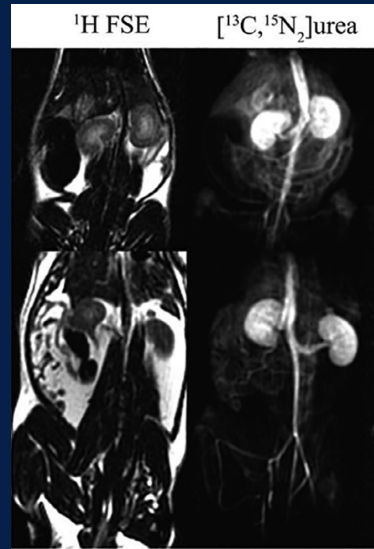
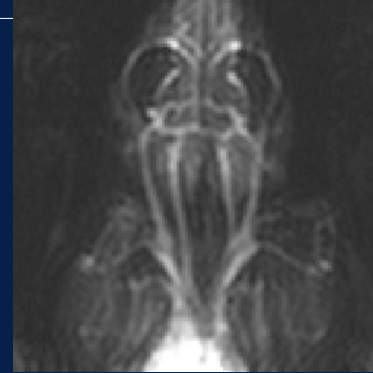


¹von Morze et al., MRM 72: 2014.

²Reed et al., IEEE TMI 33(2): 2014.

bSSFP Imaging

- First used for inert substrates¹⁻⁴



¹Svensson et al., MRM 2003.

³Hansen et al., MRM 2016.

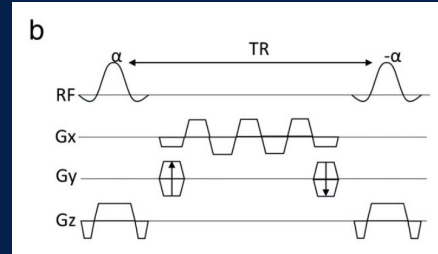
²Johansson et al., MRM 2004.

⁴Reed et al., IEEE TMI 2014.

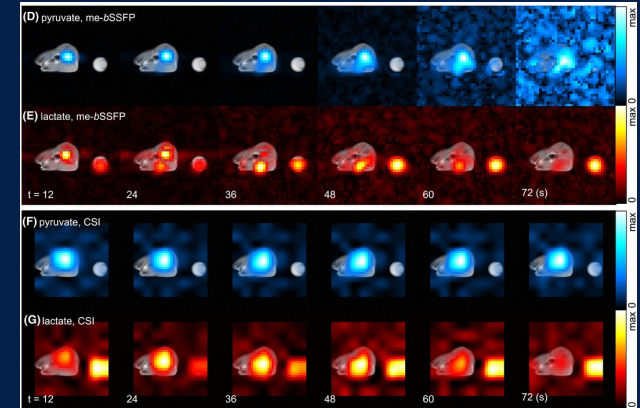
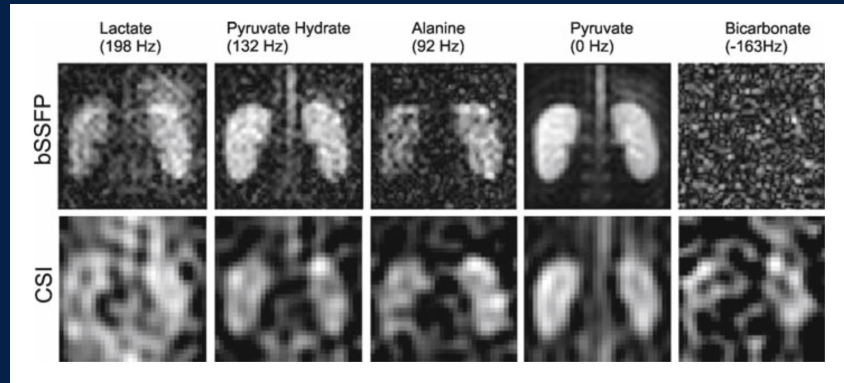
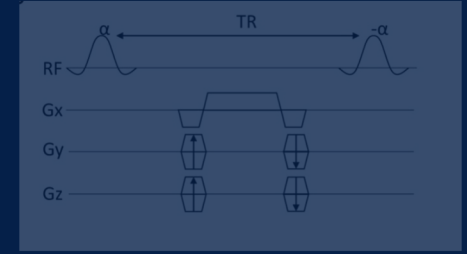
bSSFP Imaging

- First used for inert substrates¹⁻⁴
- Can also be applied to metabolically-active compounds⁵⁻⁹

Model-Based



Metabolite-Selective



¹Svensson et al., MRM 2003.

³Hansen et al., MRM 2016.

⁵Leopold et al., MRM 2009.

²Johansson et al., MRM 2004.

⁴Reed et al., IEEE TMI 2014.

⁶Müller et al., NMR in Biomed 2020.

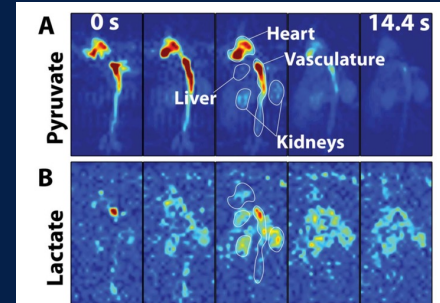
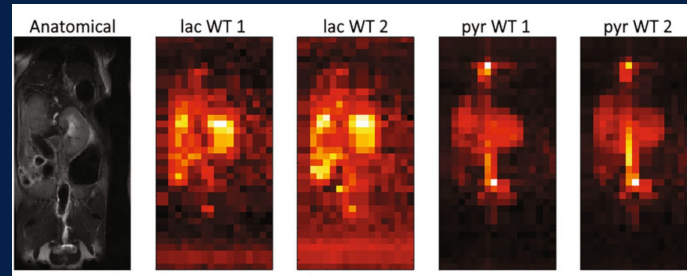
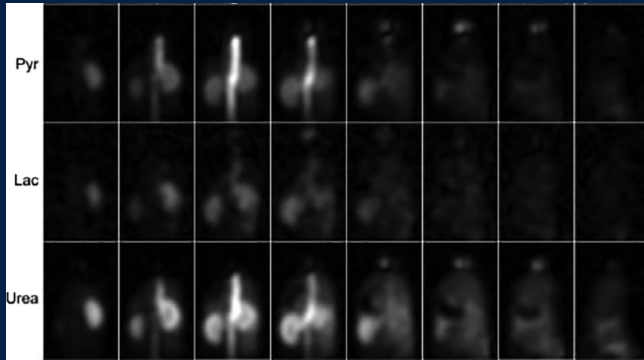
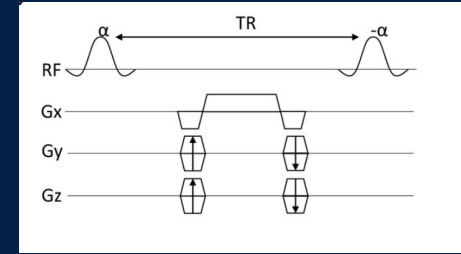
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- First used for inert substrates¹⁻⁴
- Can also be applied to metabolically-active compounds⁵⁻⁹

Model-Based



Metabolite-Selective



¹Svensson et al., MRM 2003.

³Hansen et al., MRM 2016.

⁵Leopold et al., MRM 2009.

⁷Milshcheyn et al., MRM 2018.

⁹Shang et al., MRM 2016.

²Johansson et al., MRM 2004.

⁴Reed et al., IEEE TMI 2014.

⁶Müller et al., NMR in Biomed 2020.

⁸Skinner et al., MRM 2023.

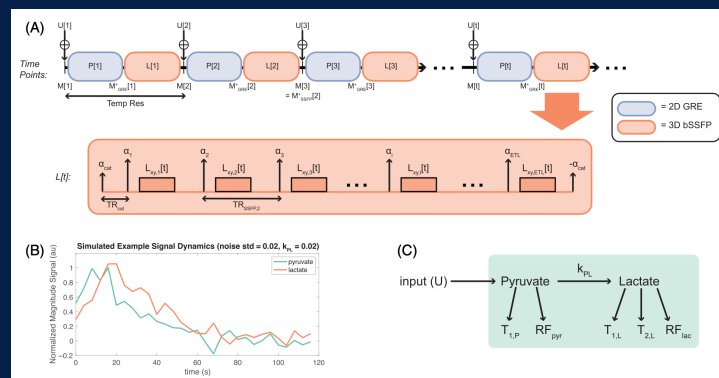
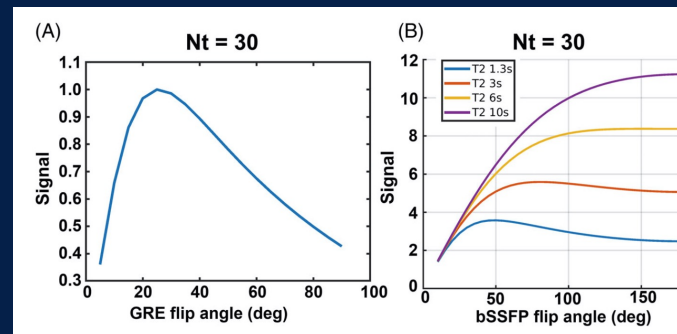
bSSFP Imaging

■ Pros:

- Highest SNR efficiency
- Compatible with model-based and metabolite-selective acquisitions

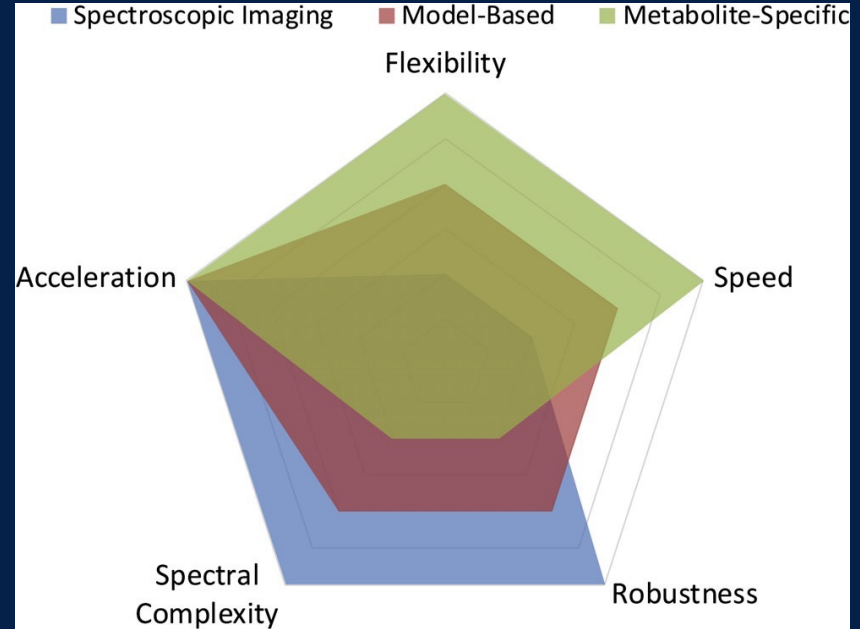
■ Cons:

- Signal is a function of many things!
 - T2/T1
 - Off-resonance
 - Banding artifacts ($\pm 1/2TR$)
- Quantification is more complicated¹



Comparison of Acquisition Schemes

- Ultimately have to decide what's the most important to you:
 - Temporal resolution?
 - Spectral bandwidth/resolution?
 - SNR efficiency?
 - Robustness?



Sequence Tradeoffs

	Pros	Cons
CSI	High spectral bandwidth High spectral resolution	Slowest Most RF inefficient Limited spatiotemporal coverage
MRSI (EPSI, Spiral CSI)	Robust to off-resonance Acquire entire spectrum No prior knowledge required	Slow Limited spectral bandwidth Limited spatiotemporal coverage
Model-Based Imaging	Rapid imaging of complex spectra Immune to B0 inhomogeneities if B0 map supplied/computed	Requires prior knowledge and accurate model of the spectrum Requires multiple RF pulses, somewhat sensitive to motion
Metabolite-Specific Imaging	Speed High SNR efficiency Robust to motion	Sensitive to off-resonance Metabolites must have sufficient chemical shift ($\sim >90$ Hz apart)

Summary & Conclusions

- Multitude of options for acquiring hyperpolarized data
- Think about your substrate-specific considerations – each sequence has strengths/weaknesses
 - CSI/MRSI: Robust. Good for crowded spectra, spectral complexity, or when peaks are not known. Limited spatial/temporal resolution
 - Model-based/metabolite-selective: Requires *a priori* knowledge, well-resolved spectrum. Faster, more coverage.
- Human [1-¹³C]pyruvate imaging has shifted away from 2D CSI and EPSI and toward faster model-based and metabolite-selective acquisitions
- Good review/overview articles on HP Imaging Strategies:
 - *Durst et al - Comparison of acquisition schemes for hyperpolarised ¹³C imaging*
 - *Gordon et al - Fast Imaging for Hyperpolarized MR Metabolic Imaging*