

# Higher, faster, smaller: Pushing the limits of fMRI at ultra-high field

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#### Acknowledgement of Country

The University of Queensland (UQ) acknowledges the Traditional Owners and their custodianship of the lands on which we meet.

We pay our respects to their Ancestors and their descendants, who continue cultural and spiritual connections to Country.

We recognise their valuable contributions to Australian and global society.





- 'Higher' fMRI at 7T offers multiple advantages
  - Higher signal-to-noise ratio (SNR)<sup>1,2,3</sup>



<sup>1</sup>Edelstein, 1986; <sup>2</sup>Pohmann, 2016; <sup>3</sup>Triantafyllou, 2005; <sup>4</sup>Gati, 1997; <sup>5</sup>Okada, 2005; <sup>6</sup>van der Zwaag, 2009; <sup>7</sup>Pruessmann, 1999; <sup>8</sup>Wald, 2012, <sup>9</sup>Hillmann, 2104; <sup>10</sup>Iadecola, 2017; <sup>11</sup>Hillman, 2007; <sup>12</sup>Ts'o, 1990; <sup>13</sup>Norris, 2006; <sup>14</sup>Tian, 2010; <sup>15</sup>Gagnon, 2015



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  - Higher functional contrast<sup>4,5,6</sup>



van der Zwaag et al., NI, 2009

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  - More acceleration<sup>7,8</sup>





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  - More acceleration<sup>7,8</sup>
- 'Smaller' neurovascular responses are tightly controlled<sup>9,10</sup>
  - Evidence of depth-dependent<sup>11</sup> and topographic<sup>12</sup> hemodynamic specificity



Ts'o et al., 1990



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- 'Smaller' neurovascular responses are tightly controlled<sup>9,10</sup>
  - Evidence of depth-dependent<sup>11</sup> and topographic<sup>12</sup> hemodynamic specificity
- 'Faster' immediate neurovascular responses<sup>9,10</sup>
  - Time to peak ~ 5 seconds<sup>13</sup>
  - Response onset < 500 ms<sup>11,14,15</sup>





<sup>1</sup>Edelstein, 1986; <sup>2</sup>Pohmann, 2016; <sup>3</sup>Triantafyllou, 2005; <sup>4</sup>Gati, 1997; <sup>5</sup>Okada, 2005; <sup>6</sup>van der Zwaag, 2009; <sup>7</sup>Pruessmann, 1999; <sup>8</sup>Wald, 2012, <sup>9</sup>Hillmann, 2104; <sup>10</sup>Iadecola, 2017; <sup>11</sup>Hillman, 2007; <sup>12</sup>Ts'o, 1990; <sup>13</sup>Norris, 2006; <sup>14</sup>Tian, 2010; <sup>15</sup>Gagnon, 2015



#### Pushing the limits of fMRI at ultra-high field





# Fast fMRI

#### Acquisition: Echo-Planar Imaging (EPI)





• One slice is excited and the complete 2D k-space is read out in a couple of tens of milliseconds



<sup>1</sup>Mansfield, 1977, J Phys C Solid State Phys



# Fast fMRI

#### Acquisition: Simultaneous Multislice (SMS)





#### Simultaneous Multislice (SMS) / Multiband<sup>1,2</sup>



#### Uğurbil, 2013, NI





#### Simultaneous Multislice (SMS) / Multiband<sup>1,2,3</sup>



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<sup>1</sup>Maudsley, 1980, JMR; <sup>2</sup>Müller, 1988, MRM; <sup>3</sup>Larkman et al., 2001, JMRI; <sup>4</sup>Breuer et al., 2005, MRM, <sup>5</sup>Setsompop et al., 2012, MRM <sup>13</sup>



#### Simultaneous Multislice (SMS) / Multiband<sup>1,2,3</sup>



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#### Simultaneous Multislice (SMS) / Multiband – Success







MULTIBAND EPI



Feinberg et al., 2010, PLoS ONE

Uğurbil et al., 2013, NI



## Simultaneous Multislice (SMS) / Multiband – Summary

#### Advantages

- Increased SNR efficiency  $(\sqrt{N})$
- Increased sampling rate

#### Disadvantages

- g-factor penalty
- Slice-leakage



Uğurbil, 2013, NI



# Fast fMRI

#### Analysis: Spatial correlations







#### False-Positive Activation due to Signal Leakage between Simultaneously Excited Slices



Todd et al., 2016, NI

@ 3T with 32-channel coil, GRAPPA 2<sup>18</sup>



# Strong Variability in Resting-State Networks at High Acceleration Factors

	M1	M2	M3	M4		M1	M2	M3	M4
pDMN					Motor				
Auditory					Visual	s F	P		·
Somatosens					Salience				

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Preibisch et al., 2015, PLOS One

@ 3T with 32-channel coil, SENSE 2 19



#### Slice-Leakage in the HCP 100 Release<sup>1</sup> 81 out of 96

motor task



As much acceleration as necessary, as little as possible!



Split slice-GRAPPA<sup>2</sup> necessary to reduce slice leakage

<sup>1</sup>Risk et al., 2018, NI; <sup>2</sup>Cauley et al., 2014, MRM



# Fast fMRI

#### Analysis: Temporal correlations







#### Temporal (Serial, Auto)-Correlation of the Noise

 Increased number of sampling points does not increase the degrees of the freedom at the same rate, because of serial correlations in the noise<sup>1</sup>



Moeller et al., 2010, MRM; Same TR and number of volumes



Feinberg et al., 2010, PloS ONE; Mixture-modelling



#### Increased false-positive rates<sup>1,2,3,4,5</sup>

Chen et al., 2019, NI



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<sup>1</sup>Eklund et al., 2012, NI; <sup>2</sup>Sahib et al., 2016, MRM; <sup>3</sup>Bollmann et al., 2018, NI; <sup>4</sup>Corbin et al., 2018, HBM; <sup>5</sup>Olszowy et al., 2019, Nat Com



#### Noise Spectrum in Fast Acquisitions



Bollmann et al., 2018, NI

#### Better pre-whitening performance

- AFNI: ARMA(1,1)
- SPM: FAST



#### On the Analysis of Rapidly Sampled fMRI Data<sup>1</sup>

Task

Normalized statistical gains in 'GLM-based task activation'



#### More statistical gains for

• Faster task



#### On the Analysis of Rapidly Sampled fMRI Data<sup>1</sup>

#### Task



#### More statistical gains for

- Faster task
- Less white noise



#### On the Analysis of Rapidly Sampled fMRI Data<sup>1</sup>

#### Task



#### More statistical gains for

- Faster task
- Less white noise
- Less serial correlations



# Fast fMRI

#### Analysis: Dynamic stimuli





# Fast fMRI Can Detect Oscillatory Neural Activity in Humans1resolution 2.5 mm isoTR = 246 ms





## High-resolution fMRI Acquisition: 3D-EPI

























































## High-resolution fMRI acquisition

- high-resolution fMRI  $\rightarrow$  sub-millimetre resolution
- majority of studies utilize a 3D EPI acquisition
  - higher temporal SNR than 2D at sub-millimetre resolution<sup>1</sup>



• higher temporal SNR than 2D at sub-millimetre resolution<sup>3,4</sup>





## High-resolution fMRI acquisition

- high-resolution fMRI  $\rightarrow$  sub-millimetre resolution
- majority of studies utilize a 3D EPI acquisition
  - higher temporal SNR than 2D at sub-millimetre resolution<sup>1</sup>
  - low SAR/better slice profile
- current parameter 'optimum'
  - 0.7 1 mm resolution
  - 25 35 ms TE
  - 2-3 s TR (partial coverage)
  - R = 4
  - 6/8 no PF
- current limitations
  - image fidelity (blurring & B<sub>0</sub>)
  - resolution/TE

G) 0.79 mm T  $_2^*$  (functional EPI)



Huber et al., NI, 2020



# High-resolution fMRI

#### **Cortical architecture**











#### Coordinate system for high-resolution fMRI



- 2 main partitioning axes of the cortex<sup>1</sup>
  - perpendicular to the surface → laminar (= depth-dependent)<sup>2</sup>
  - parallel to the surface → columnar (= topographic)<sup>3</sup>

<sup>1</sup>Harris and Mrsic-Flogel, Nature, 2013; Shamir and Assaf, medRxiv, 2020

<sup>2</sup>Barth and Norris, NMR Biomed, 2007; Polimeni et al., NI, 2010; Olman et al., PlosOne, 2012; Huber et al., Neuron, 2017
<sup>3</sup>Engel et al., Nature, 1994; Sereno et al., Science, 1995; Wandell et al., Neuron, 2007; Silver and Kastner, Trends in Cogn Sciences, 2009; Sanchez-Panchuelo et al., J Neurosci, 2012; Besle et al., J Neurphysiology, 2013; Puckett et al., Neuroimage, 2017; Wessinger et al., HBM, 1997; Bilecen et al., Hearing Research. 1998; Talavage et al., J Neurphysiology, 2004; 45



# High-resolution fMRI Analysis: Topographic analysis



#### Ocular dominance columns



Cheng et al., Neuron, 2001

Menon et al., J Neurophysiol, 1997



Nasr et al., J Neurosci, 2016



#### Attention in somatosensory cortex



Puckett et al., NI, 2017



## **High-resolution fMRI**

#### Analysis: Depth-dependent analysis





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Amunts et al., Science, 2013 Logothetis, Science, 2008



# An increase in % BOLD signal change is commonly observed across cortical depths





#### Sources of the pial bias

#### Pial veins



#### Or intracortical veins?





0.5

cortical depth

IV

Cortical depth (mm)

Fracasso et al., NI, 2018

Chen et al., NI, 2013

voxel sorting

0.5



Kok et al., Current Biology, 2016 experimental design

weak

middle

strong

superficial

superficial

14 ·

8

2

%

0.5

**|~|||** 

0

53

V/VI

15



#### Beyond vasculature: acquisition and analysis challenges<sup>1,2,3</sup>

#### <u>Acquisition</u>

- Distortions due to B<sub>0</sub> inhomogeneities
- $T_2^*$  blurring
- Partial Fourier

#### <u>Analysis</u>

- Registration of structural and functional images
- GM/WM and GM/CSF boundary definition
- Definition of 'depth'



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