

Data-driven, model-free, deep learning approach for quantitative MRI protocol design

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Outline of the talk



- Introduction
 - *quantitative MRI (qMRI)*
 - *qMRI protocol optimisation*

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 - *signal prediction: MUDI challenge*
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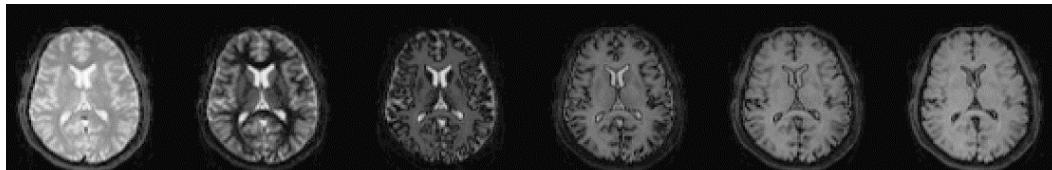
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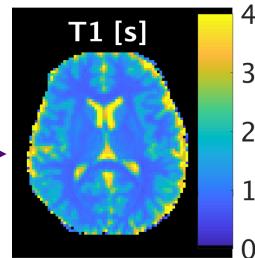
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- Discussion and conclusions

Introduction: qMRI

- In quantitative MRI (qMRI), sets of multi-contrast images are analysed to estimate biophysical properties of tissues in each image voxel

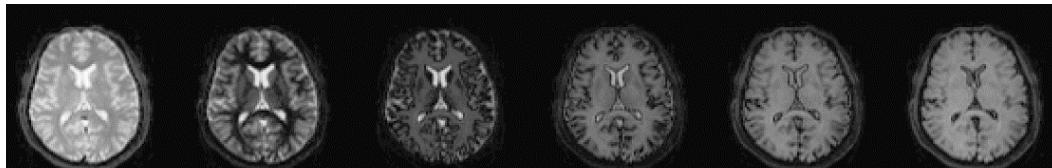


$$s = s_0 \left| 1 - 2 e^{-\frac{TI}{T1}} \right|$$

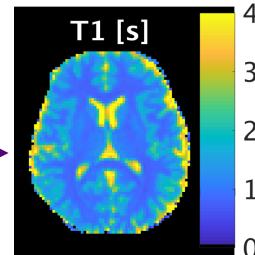


Introduction: qMRI

- In quantitative MRI (qMRI), sets of multi-contrast images are analysed to estimate biophysical properties of tissues in each image voxel



$$s = s_0 \left| 1 - 2 e^{-\frac{TI}{T1}} \right|$$



- **qMRI protocol:** set of sequence parameter settings to use to produce such a multi-contrast MRI acquisition
- e.g., $TI = \{80\text{ms}, 160\text{ms}, 320\text{ms}, 640\text{ms}, 1280\text{ms}, 2560\text{ms}\}$

Model-based protocol optimisation



- **Optimisation** → find a protocol that is *optimum* according to some criterion

Model-based protocol optimisation



- **Optimisation** → find a protocol that is *optimum* according to some criterion
- **Model-based approach** → *optimality* is based on an explicit signal model [1]

Model-based protocol optimisation



- **Optimisation** → find a protocol that is optimum according to some criterion
- **Model-based approach** → *optimality* is based on an explicit signal model [1]
 1. Define the signal model, e.g., $s = \sum_n^N f_n e^{-b D_n}$
 2. Define the expected distribution of tissue parameters $\mathbf{p} = (f_1, D_1, f_2, D_2, \dots)$
 3. Define the noise level σ
 4. Define an optimality criterion, e.g., minimum Cramer-Rao Bound $J^{-1}(b; \mathbf{p}, \sigma)$
 5. Find M sequence parameter configurations that maximise optimality:

$$(b_1, b_2, \dots, b_M) = \arg \min_{\mathbf{p}} \sum J^{-1}(b; \mathbf{p}, \sigma)$$

Data-driven protocol optimisation



- **Model-based protocol optimisation comes with assumptions**
 - *the signal model itself*
 - *the range of variation of tissue parameters*
 - *the noise level*

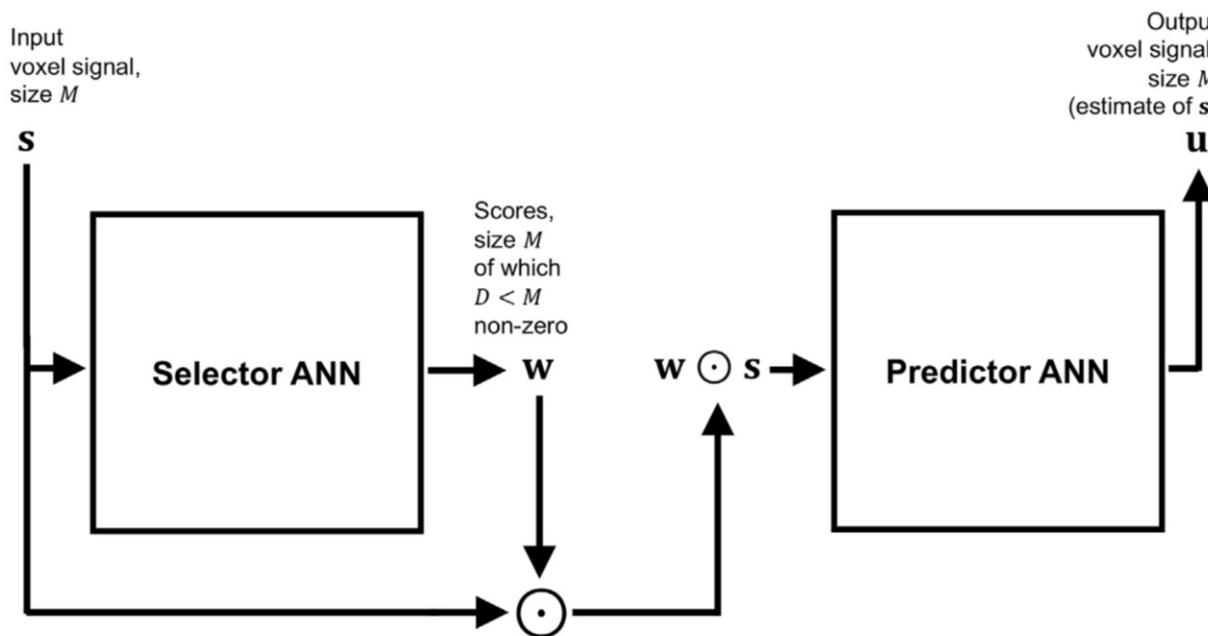
Data-driven protocol optimisation



- **Model-based protocol optimisation comes with assumptions**
 - *the signal model itself*
 - *the range of variation of tissue parameters*
 - *the noise level*
- **Data-driven optimisation** → learn compact protocols from rich pilot scans
 - *no assumptions on signal models, tissue parameters, noise levels*
 - *test scans are commonly performed when setting up new studies*
 - *useful when the model of interest is not known/fixed*

The SARDU-Net framework

Select And Retrieve via Direct Upsampling Network (SARDU-Net)



- 1) Perform a few rich qMRI acquisitions of M measurements
- 2) Find a maximally informative subset of $D < M$ measurements
- 3) Use the qMRI protocol of size D for your prospective study

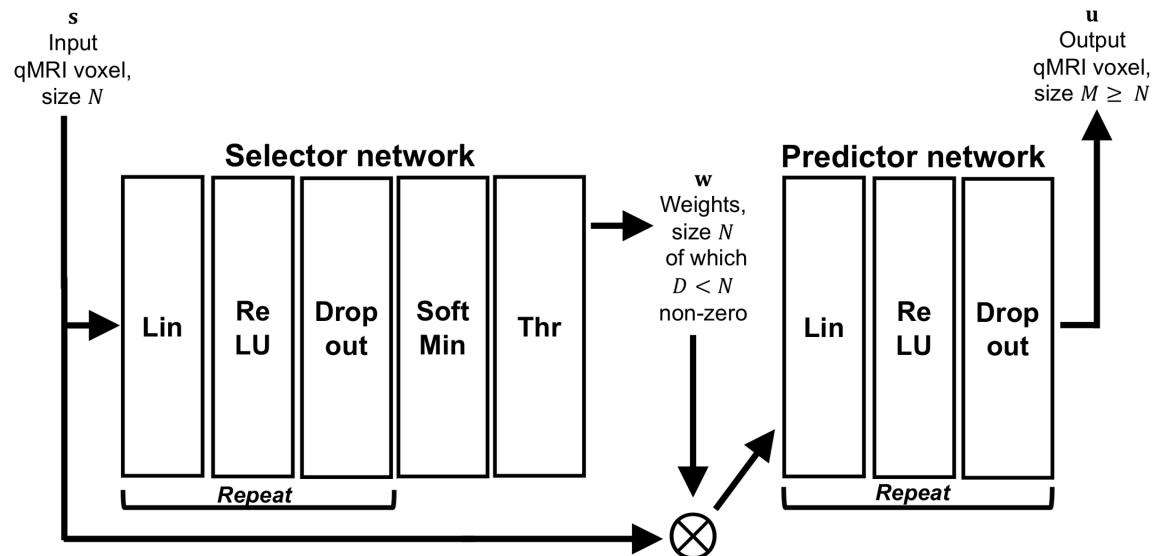
Selector and Predictor networks

Architecture

- Multi-layer, fully-connected feedforward networks implemented in PyTorch

Network training

- Loss based on the signal reconstruction error
 $\rightarrow L = \| s - u(s \odot w) \|_2^2$
- ADAM optimiser [3] with dropout regularisation



[3] Kingma DP and Ba J. Proc 3rd Int Conf Learn Represent (2015), <http://arxiv.org/abs/1412.6980>

SARDU-Net demonstration: brain MRI (1)



3 healthy subjects scanned on a 3T Philips Ingenia CX

- saturation inversion recovery (SIR) [4] diffusion-weighted (DW) spin echo EPI
- 528 images with 32 unique (b ,TI)
 - $b = \{0, 1000, 2000, 3000\} \text{ s/mm}^2$
 - $\text{TI} = \{70, 320, 570, 820, 1070, 1320, 1570, 1820\} \text{ ms}$
 - 21 directions per (b ,TI)
- TS = 300 ms (saturation time)
- TE = 90 ms
- TR = 2563 ms
- 2.4 mm isotropic resolution
- SENSE = 2
- Multiband factor = 3
- Scan time = 45 min

SARDU-Net demonstration: brain MRI (2)



- Find subsets of $D = \{4, 8, 16\}$ out of $M = 32$ measurements
- Fit a model of diffusion-T1 relaxation [5,6] ...

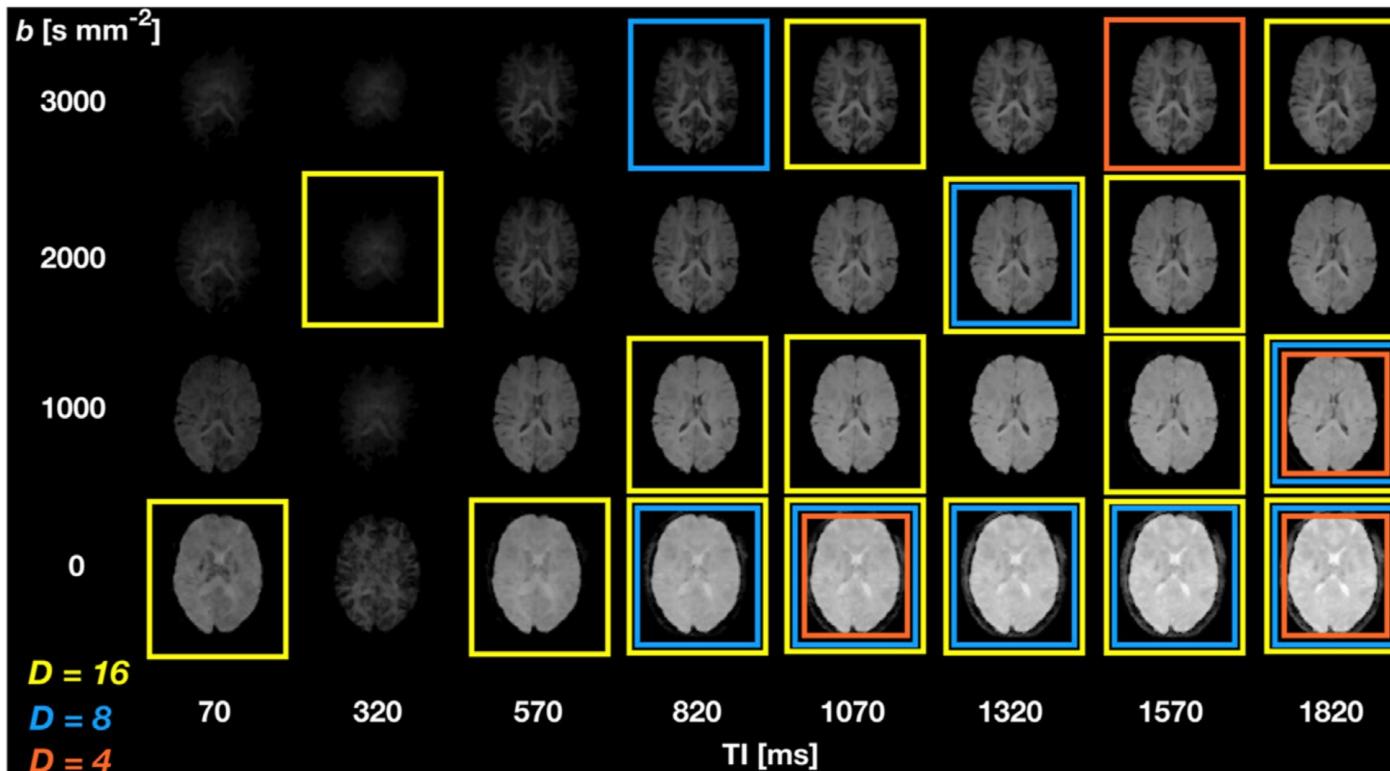
$$s(b, \text{TI}, \text{TS}) = \frac{\sqrt{\pi}}{2} s_0 \left| 1 - e^{-\frac{\text{TI}}{T_1}} - \left(1 - e^{-\frac{\text{TS}}{T_1}} \right) e^{-\frac{\text{TI}}{T_1}} \right| e^{-bd_{\perp}} \frac{\operatorname{erf}\left(\sqrt{b(d_{\parallel} - d_{\perp})}\right)}{\sqrt{b(d_{\parallel} - d_{\perp})}}$$

- ... and predict fully-sampled signals based on the fitted parameters
- Assess the quality of reconstructed signals/metrics against:
 - *random sub-protocols*
 - *uniform down-sampling*
 - *geometric down-sampling*

[5] De Santis S et al, *NeuroImage* 2016, doi:10.1016/j.neuroimage.2016.07.037

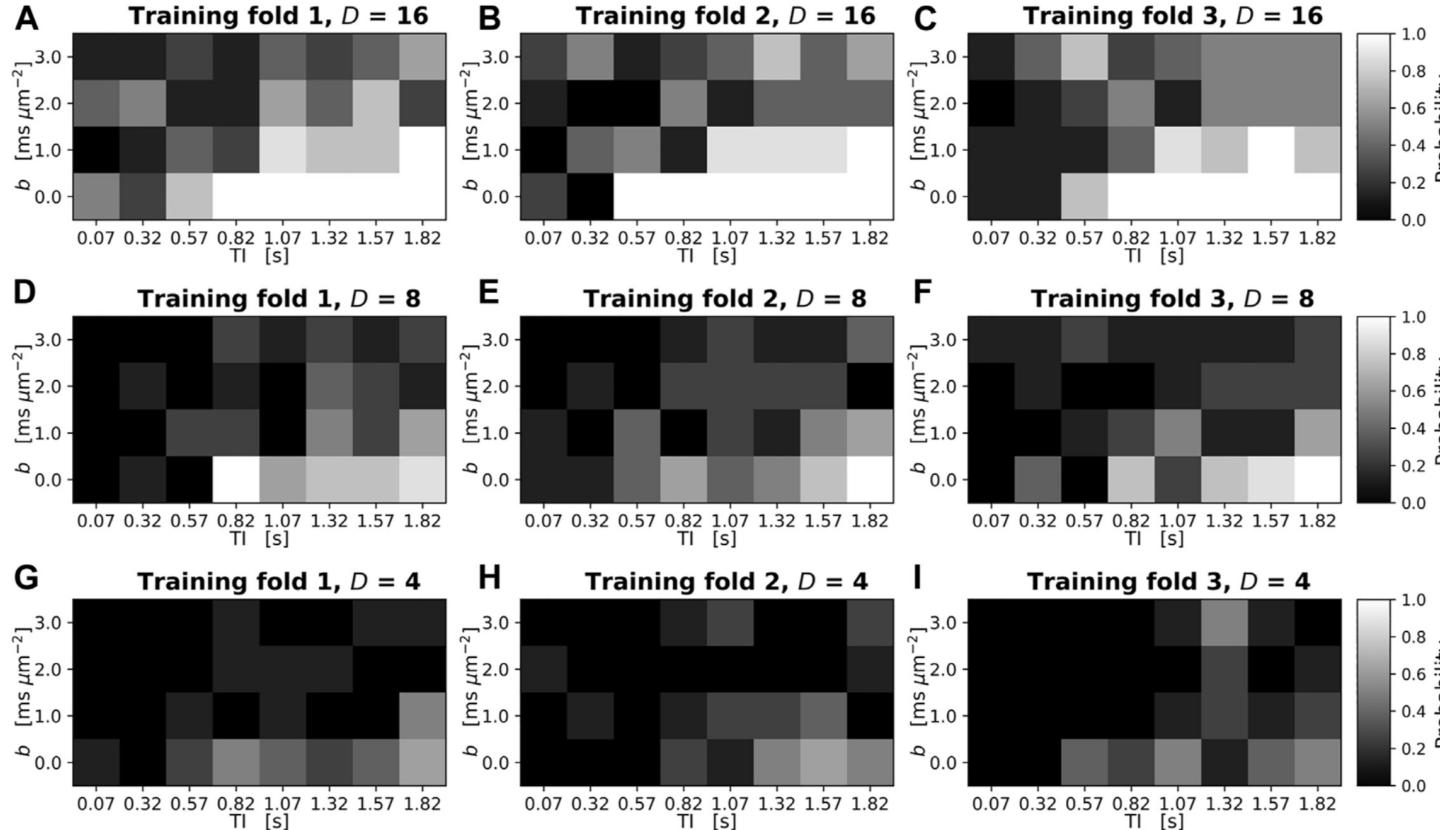
[6] Kaden E et al, *Magn Reson Med* 2016, doi:10.1002/mrm.25734

Results: brain sub-protocol selection



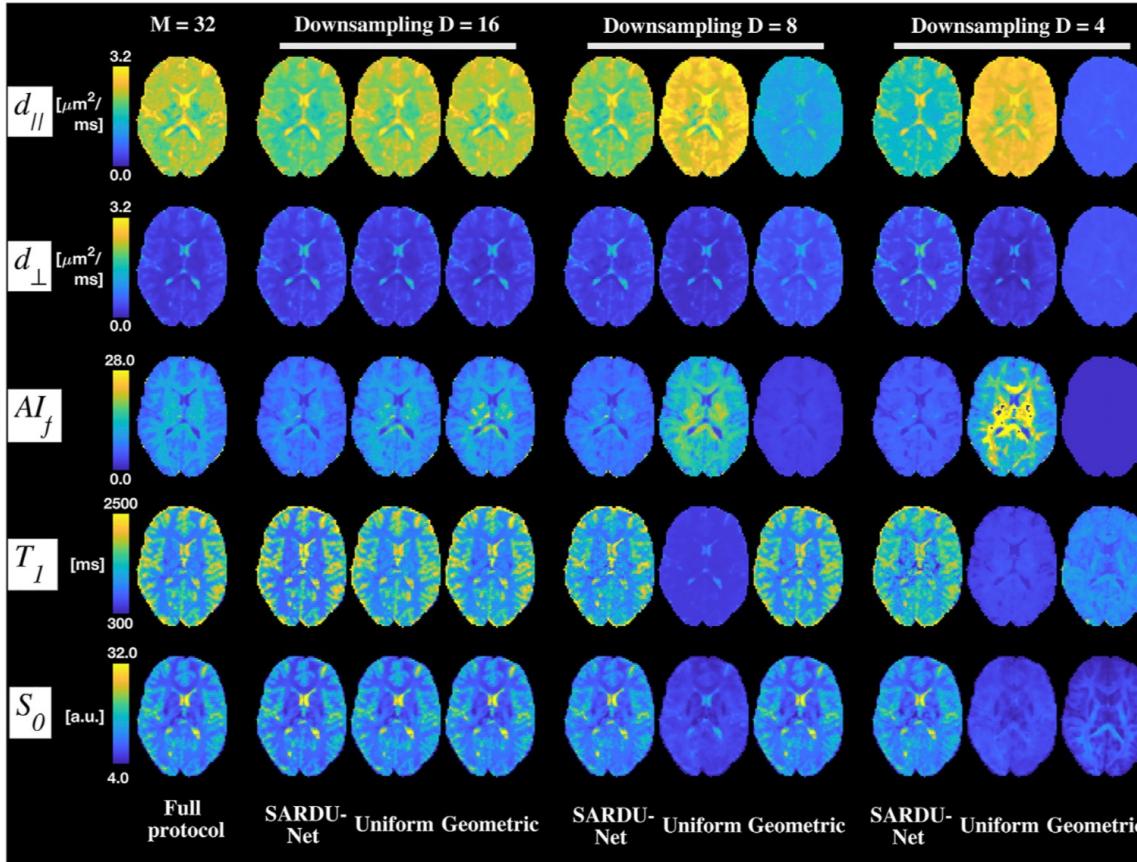
- A variety of contrasts are sampled
- SNR plays a role, but high b -values are always selected

Results: selection reproducibility



- Sub-protocol selection consistent across training folds and initialisations
- Some variability is seen

Results: parametric maps



- For low sub-sampling rates, uniform and geometric sub-protocols work just fine
- For aggressive sub-sampling, SARDU-Net sub-protocols enable better map computation

Results: differences w. r. t. reference

TABLE 1 | Results of the SARDU-Net, uniform and geometric sub-protocol comparison against a null distribution from randomly selected sub-protocols (brain data, T1-SMDT model).

D/M	Sub-sampling	Signal MSE [a.u.]			d_{\parallel} difference [$\mu\text{m}^2 \text{ ms}^{-1}$]			d_{\perp} difference [$\mu\text{m}^2 \text{ ms}^{-1}$]			T_1 difference [ms]			s_0 difference [a.u.]		
		Subj. 1	Subj. 2	Subj. 3	Subj. 1	Subj. 2	Subj. 3	Subj. 1	Subj. 2	Subj. 3	Subj. 1	Subj. 2	Subj. 3	Subj. 1	Subj. 2	Subj. 3
16/32	SARDU-Net	0.162 (q=0.003)*	0.104 (q=0.09)	0.195 (q=0.001)*	-0.048 (q=0.63)	-0.018 (q=0.12)	0.026 (q=0.23)	0.026 (q=0.91)	0.028 (q=0.82)	0.017 (q=0.72)	13.2 (q=0.33)	9.2 (q=0.20)	21.1 (q=0.25)	0.384 (q=0.33)	0.238 (q=0.25)	0.540 (q=0.20)
	Uniform	0.170 (q=0.24)	0.105 (q=0.23)	0.204 (q=0.19)	0.005 (q=0.06)	0.019 (q=0.13)	-0.023 (q=0.21)	-0.008, (q=0.47)	-0.012 (q=0.56)	-0.010 (q=0.48)	6.0 (q=0.17)	-7.6 (q=0.17)	-3.7 (q=0.03)*	0.221 (q=0.19)	-0.157 (q=0.19)	-0.453 (q=0.14)
	Geometric	0.177 (q=0.43)	0.107 (q=0.36)	0.224 (q=0.58)	0.028 (q=0.44)	0.019 (q=0.13)	0.051 (q=0.39)	0.002 (q=0.12)	-0.003 (q=0.17)	0.007 (q=0.39)	-19.1 (q=0.46)	18.0 (q=0.39)	-7.9 (q=0.08)	0.410 (q=0.36)	0.229 (q=0.24)	0.082 (q=0.02)*
	95% range	[0.165; 0.482] [0.103; 0.565] [0.199; 0.584]	[0.103; 0.086] [0.199; 0.086]	[0.224; 0.146] [0.224; 0.178]	[−0.121; 0.146] [−0.121; 0.146]	[−0.207; 0.178] [−0.207; 0.178]	[−0.258; 0.202] [−0.258; 0.202]	[−0.040; 0.024] [−0.040; 0.024]	[−0.093; 0.024] [−0.093; 0.024]	[−0.061; 0.024] [−0.061; 0.024]	[−177.4; 63.1] [−177.4; 63.1]	[−214.7; 88.4] [−214.7; 88.4]	[−274.0; 71.9] [−274.0; 71.9]	[−7.088; 1.439] [−7.088; 1.439]	[−9.902; 1.212] [−9.902; 1.212]	[−9.54; 1.29] [−9.54; 1.29]
8/32	SARDU-Net	0.182 (q=0.05)*	0.116 (q=0.12)	0.214 (q=0.04)*	-0.033 (q=0.26)	0.127 (q=0.53)	0.021 (q=0.09)	0.045 (q=0.82)	0.002 (q=0.04)*	0.032 (q=0.57)	37.8 (q=0.40)	20.8 (q=0.23)	53.0 (q=0.36)	0.970 (q=0.37)	0.083 (q=0.04)*	0.992 (q=0.28)
	Uniform	0.343 (q=0.84)	0.203 (q=0.61)	0.558 (q=0.78)	0.018 (q=0.13)	0.027 (q=0.10)	-0.039 (q=0.16)	-0.027 (q=0.61)	-0.038 (q=0.55)	-0.037 (q=0.60)	455.8 (q=0.99)	547.9 (q=0.99)	351.9 (q=0.99)	18.01 (q=0.99)	18.27 (q=0.99)	12.20 (q=0.97)
	Geometric	0.235 (q=0.28)	0.189 (q=0.52)	0.294 (q=0.32)	-0.471 (q=0.98)	-0.486 (q=0.97)	-0.500 (q=0.97)	0.064 (q=0.91)	0.014 (q=0.27)	0.054 (q=0.74)	8.2 (q=0.14)	43.5 (q=0.40)	26.0 (q=0.17)	0.463 (q=0.18)	0.929 (q=0.41)	0.985 (q=0.28)
	95% range	[0.177; 1.483] [0.107; 2.140] [0.215; 1.984]	[0.107; 2.140] [0.107; 2.140]	[0.215; 1.984] [0.215; 1.984]	[−0.350; 0.344] [−0.425; 0.384]	[−0.425; 0.384] [−0.498; 0.391]	[−0.498; 0.391] [−0.084; 0.053]	[−0.084; 0.053] [−0.147; 0.042]	[−0.147; 0.042] [−0.111; 0.053]	[−0.111; 0.053] [−281.7; 109.0]	[−265.5; 146.5] [−265.5; 146.5]	[−339.5; 92.2] [−339.5; 92.2]	[−11.76; 2.825] [−11.76; 2.913]	[−12.32; 2.107] [−12.32; 2.107]	[−12.26; 2.107] [−12.26; 2.107]	
4/32	SARDU-Net	0.202 (q=0.002)*	0.122 (q=0.01)*	0.235 (q=0.001)*	0.016 (q=0.05)*	-0.210 (q=0.35)	0.093 (q=0.16)	0.035 (q=0.41)	0.045 (q=0.28)	0.046 (q=0.38)	53.6 (q=0.24)	81.8 (q=0.29)	99.5 (q=0.30)	1.56 (q=0.20)	1.46 (q=0.15)	2.46 (q=0.24)
	Uniform	0.689 (q=0.55)	0.500 (q=0.52)	0.649 (q=0.50)	-0.181 (q=0.39)	-0.211 (q=0.35)	-0.218 (q=0.36)	-0.002 (q=0.03)*	-0.017 (q=0.12)	-0.015 (q=0.13)	196.7 (q=0.62)	260.7 (q=0.78)	107.8 (q=0.32)	4.27 (q=0.44)	3.04 (q=0.24)	0.07 (q=0.006)*
	Geometric	1.250 (q=0.66)	1.231 (q=0.66)	1.353 (q=0.66)	-0.020 (q=0.07)	-0.033 (q=0.06)	0.039 (q=0.06)	-0.031 (q=0.37)	-0.122 (q=0.69)	-0.068 (q=0.58)	-59.7 (q=0.27)	-159.7 (q=0.53)	-213.0 (q=0.56)	-2.18 (q=0.28)	-9.92 (q=0.67)	7.67 (q=0.58)
	95% range	[0.257; 2.544] [0.138; 2.547] [0.309; 0.294]	[−1.00; 0.543] [−1.00; 0.543]	[0.309; 0.550] [0.309; 0.550]	[−1.08; 0.596] [−1.11; 0.596]	[−0.158; 0.174] [−0.218; 0.153]	[−0.190; 0.180] [−531.4; 277.9]	[−531.4; 277.9] [−501.8; 294.5]	[−643.3; 250.4] [−501.8; 250.4]	[−15.58; 8.85] [−14.48; 7.02]	[−14.48; 7.02] [−14.48; 5.24]	[−14.48; 8.85] [−14.48; 5.24]	[−14.48; 7.02] [−14.48; 5.24]	[−14.48; 7.02] [−14.48; 5.24]	[−14.48; 7.02] [−14.48; 5.24]	

For each sub-protocol and sub-sampling factor, the table reports subject-wise signal MSE and mean differences of parametric maps with respect to maps obtained from fully sampled signals via dictionary fitting. The table also reports the 95% inclusion ranges of the random sub-protocol distribution, and the closest quantile from the random sub-protocol distribution to which MSEs and parametric map differences (in absolute value) correspond. The lowest MSE/parametric map differences among SARDU-Net, uniform and geometric sub-sampling is shown in bold font. Asterisks flag cases where the quantile q is $q \leq 0.05$.

- SARDU-Net sub-protocols enable the best signal reconstruction using a model they were not optimised for
- However, this does not imply that parametric maps are the closest to the reference

SARDU-Net demonstration: prostate MRI (1)



3 healthy subjects scanned on a 3T Philips Achieva

- DW spin echo EPI with variable TE
- 48 images with 16 unique (b, TE)
 - $b = \{0, 500, 1000, 1500\} \text{ s/mm}^2$
 - $\text{TE} = \{55, 87, 121, 150\} \text{ ms}$
 - 3 directions per (b, TE)
- TR = 2800 ms
- resolution: 1.75 mm \times 1.75 mm \times 5 mm
- SENSE = 1.6, partial Fourier factor = 0.62
- Scan time = 6 min

SARDU-Net demonstration: prostate MRI (2)

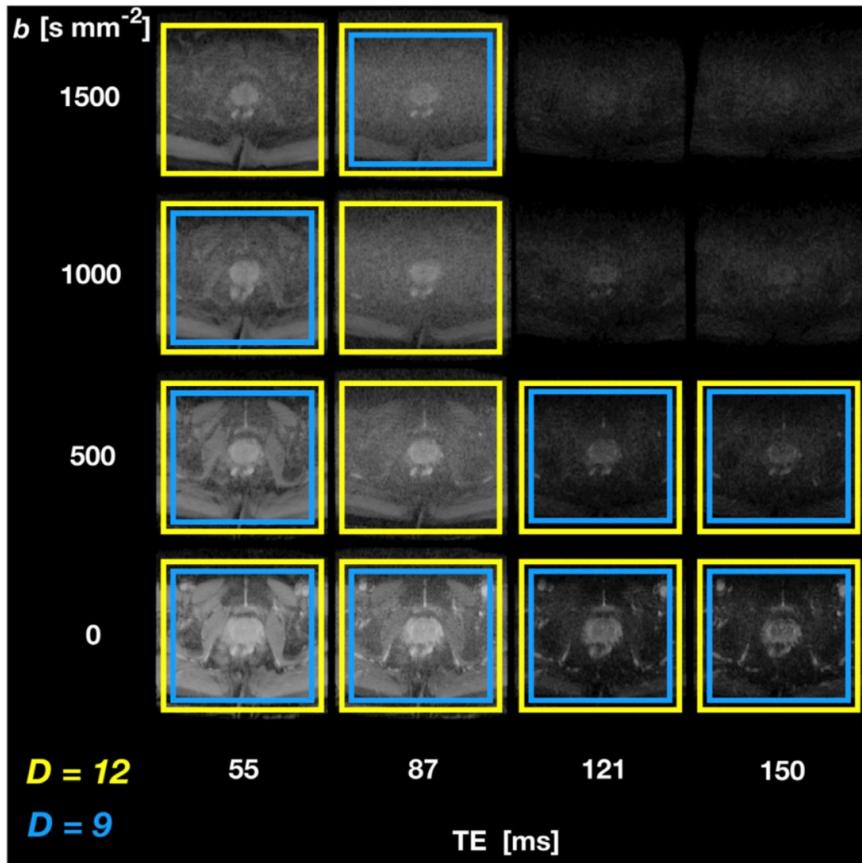


- Find subsets of $D = \{9, 12\}$ out of $M = 16$ measurements
- Fit a model of diffusion-T2 relaxation [7] ...

$$s(b, \text{TE}) = s_0 \left(\nu_l e^{-b d_l - \frac{\text{TE}}{T_{2l}}} + (1 - \nu_l) \left(\nu_e e^{-b d_e - \frac{\text{TE}}{T_{2e}}} + (1 - \nu_e) e^{-b d_s - \frac{\text{TE}}{T_{2s}}} \right) \right)$$

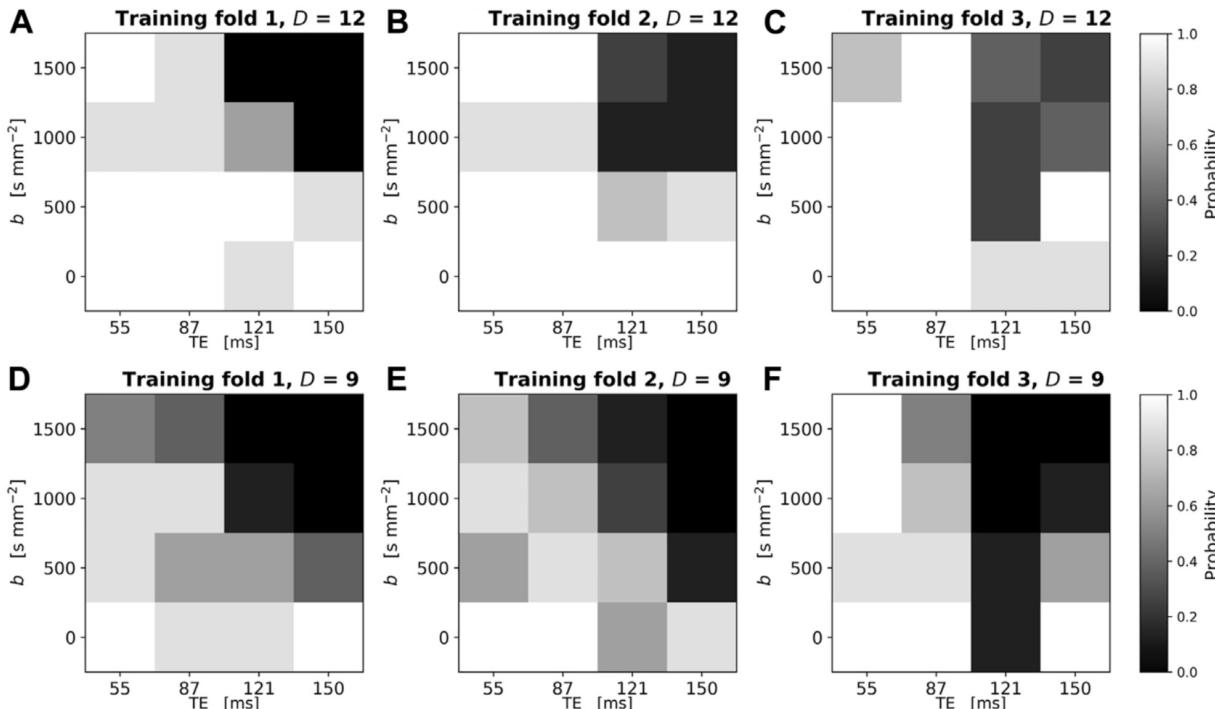
- ... and predict fully-sampled signals based on the fitted parameters
- Assess the quality of reconstructed signals/metrics against:
 - *random sub-protocols*
 - *uniform down-sampling*
 - *geometric down-sampling*

Results: prostate sub-protocol selection



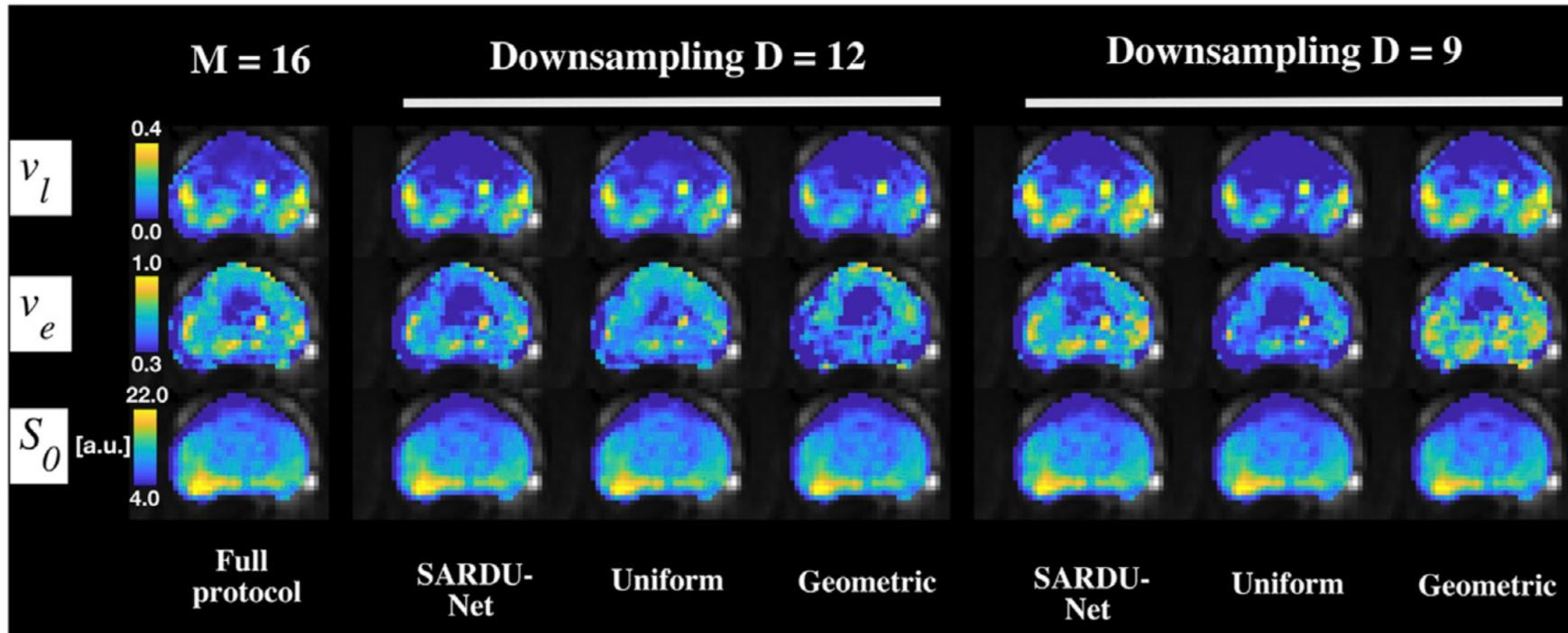
- A variety of contrasts are sampled
- SNR plays a role on measurement selection
- However, for strong subsamplings, images with lower SNR may be preferred to images with higher SNR

Results: selection reproducibility



- Sub-protocol selection consistent across training folds and initialisations
- Some variability is seen

Results: parametric maps



- Parametric maps from SARDU-Net sub-protocols have similar quality to the reference maps on visual inspection

Results: differences w. r. t. reference



TABLE 2 | Results of the SARDU-Net, uniform and geometric sub-protocol comparison against a null distribution obtained from all possible sub-protocols (prostate data, HM-MRI model). The bold font indicates the lowest MSE/lowest parametric map difference among values obtained for SARDU-Net, uniform and geometric sub-samplings.

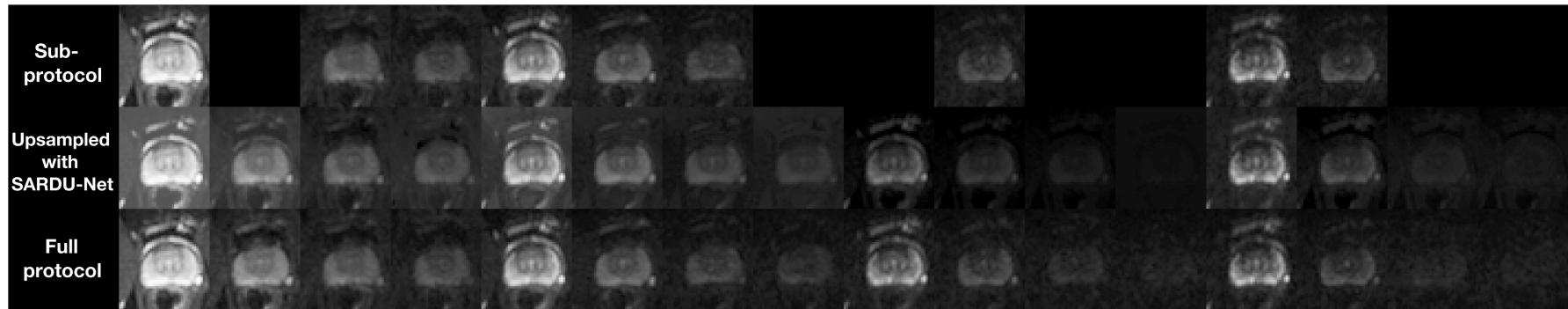
D/M	Sub-sampling	Signal MSE [a.u.]			v_t difference			v difference			s_0 difference [a.u.]		
		Subj. 1	Subj. 2	Subj. 3	Subj. 1	Subj. 2	Subj. 3	Subj. 1	Subj. 2	Subj. 3	Subj. 1	Subj. 2	Subj. 3
12/16	SARDU-Net	0.80 (q = 0.01)*	0.43 (q = 0.01)*	0.047 (q = 0.02)*	-0.0006 (q = 0.001)*	-0.001 (q = 0.02)*	-0.006 (q = 0.23)	0.01 (q = 0.04)*	0.001 (q = 0.006)*	-0.028 (q = 0.32)	0.02 (q = 0.21)	0.006 (q = 0.07)	-0.001 (q = 0.07)
	Uniform	1.13 (q = 0.88)	0.51 (q = 0.69)	0.051 (q = 0.31)	0.01 (q = 0.001)*	-0.04 (q = 0.41)	-0.012 (q = 0.40)	0.23 (q = 0.77) (q = 0.65)	-0.21 (q = 0.49)	-0.052 (q = 0.49)	-0.08 (q = 0.70)	0.079 (q = 0.64)	0.015 (q = 0.51)
	Geometric	0.90 (q = 0.16)	0.44 (q = 0.14)	0.050 (q = 0.25)	0.0005 (q = 0.001)*	-0.002 (q = 0.03)*	0.003 (q = 0.12)	0.06 (q = 0.06) (q = 0.29)	0.08 (q = 0.55)	0.062 (q = 0.67)	0.08 (q = 0.63)	0.076 (q = 0.76)	0.034
	95% range	[0.88; 2.03]	[0.44; 0.76]	[0.048; 0.080]	[0.001; 0.39]	[- 0.07; 0.16]	[- 0.05; 0.06]	[- 0.22; 0.60]	[- 0.26; 0.37]	[- 0.127; 0.220]	[- 0.12; 0.24]	[- 0.30; 0.13]	[- 0.067; 0.049]
9/16	SARDU-Net	0.88 (q = 0.01)*	0.46 (q = 0.06)	0.052 (q = 0.06)	-0.00004 (q = 0.001)*	0.088 (q = 0.69)	0.025 (q = 0.41)	0.006 (q = 0.01)*	0.23 (q = 0.51)	0.031 (q = 0.17)	-0.01 (q = 0.06)	0.04 (q = 0.17)	-0.002 (q = 0.03)*
	Uniform	1.05 (q = 0.51)	0.58 (q = 0.56)	0.058 (q = 0.25)	-0.0006 (q = 0.001)*	-0.059 (q = 0.34)	-0.026 (q = 0.42)	0.214 (q = 0.49)	-0.25 (q = 0.54)	-0.087 (q = 0.42)	-0.03 (q = 0.20)	0.12 (q = 0.55)	0.033 (q = 0.56)
	Geometric	0.97 (q = 0.35)	0.47 (q = 0.09)	0.053 (q = 0.09)	0.02 (q = 0.64)	0.048 (q = 0.28)	0.020 (q = 0.35)	-0.181 (q = 0.42)	0.09 (q = 0.21)	0.044 (q = 0.23) (q = 0.11)	-0.02 (q = 0.11) (q = 0.18)	0.05 (q = 0.18)	0.022 (q = 0.39)
	95% range	[0.89; 2.56]	[0.45; 1.27]	[0.050; 0.168]	[0.001; 0.44]	[- 0.073; 0.345]	[- 0.060; 0.167]	[- 0.251; 0.615]	[- 0.31; 0.37]	[- 0.157; 0.314]	[- 0.24; 0.60] (q = 0.24)	[- 0.40; 0.28]	[- 0.076; 0.117]

For each sub-protocol and sub-sampling factor, the table reports subject-wise signal MSE and mean differences of parametric maps with respect to maps obtained from fully sampled signals via dictionary fitting. The table also reports the 95% inclusion ranges of all sub-protocol distribution, and the closest quantile from the all sub-protocol distribution to which MSEs and parametric map differences (in absolute value) correspond. The lowest MSE/parametric map differences among SARDU-Net, uniform and geometric sub-sampling is shown in bold font. Asterisks flag cases where the quantile q is $q < 0.05$.

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- However, this does not imply that parametric maps are the closest to the reference

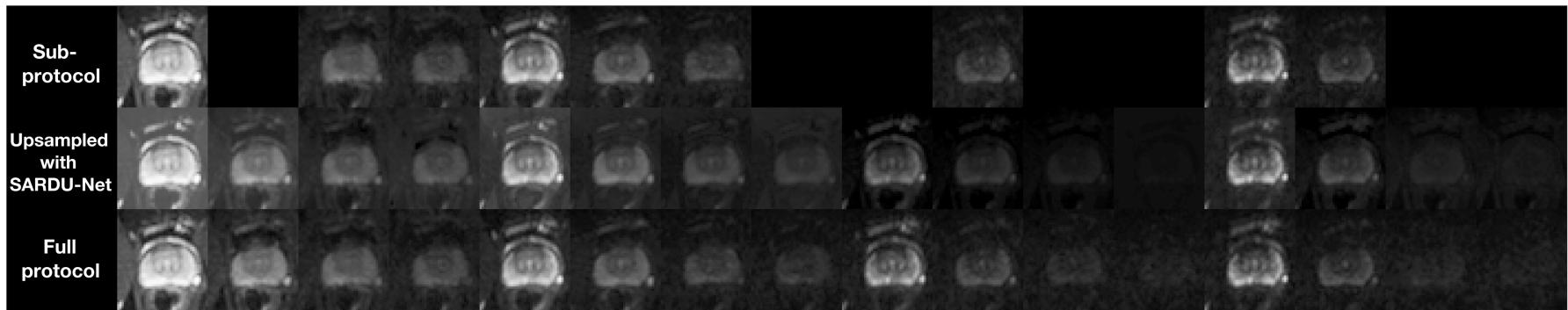
qMRI upsampling

- The Predictor module effectively learns how to up-sample in qMRI space



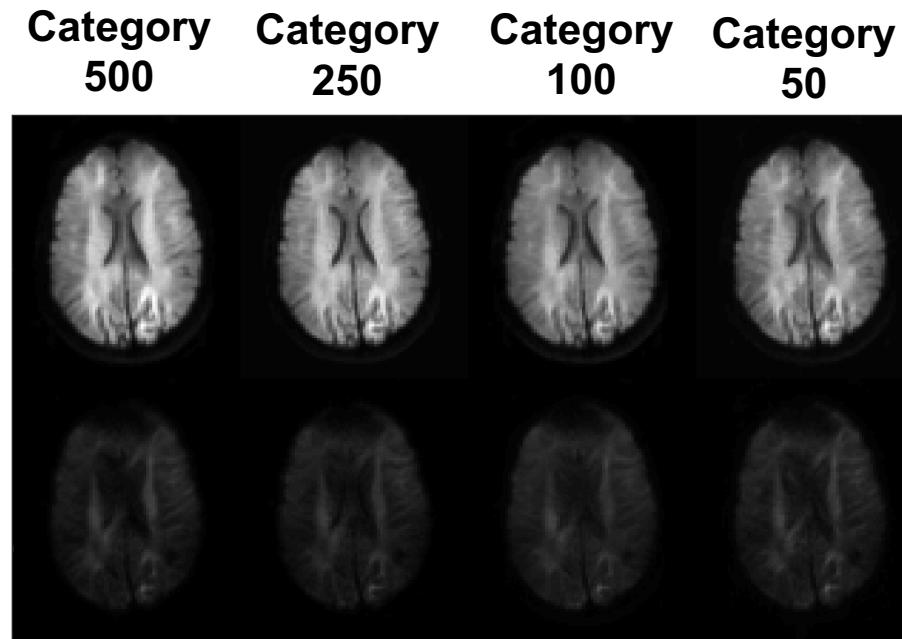
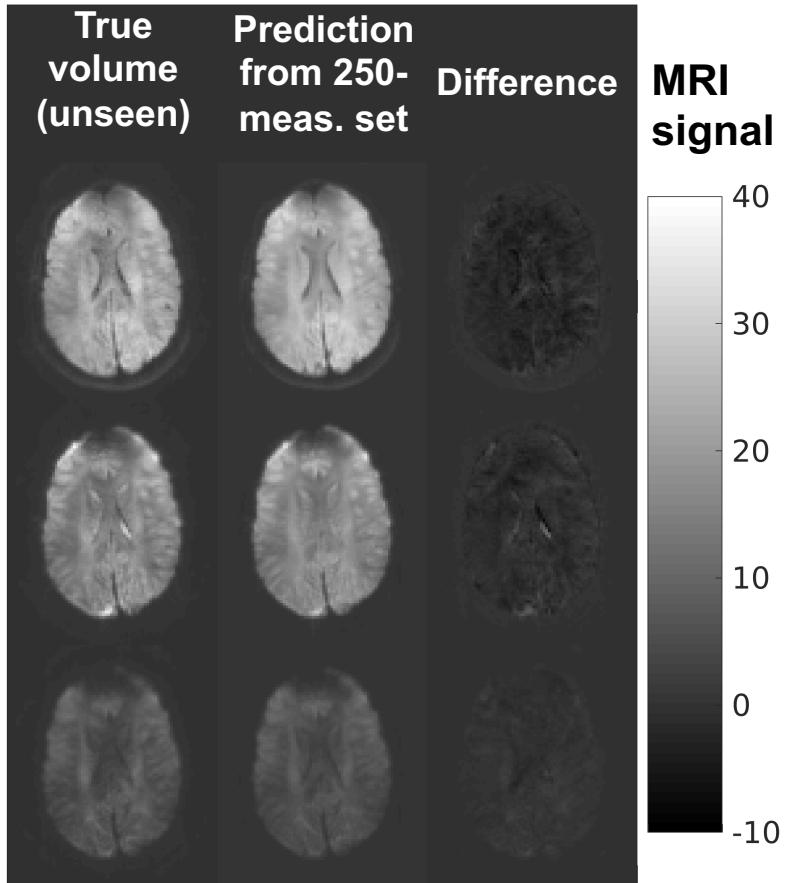
qMRI upsampling

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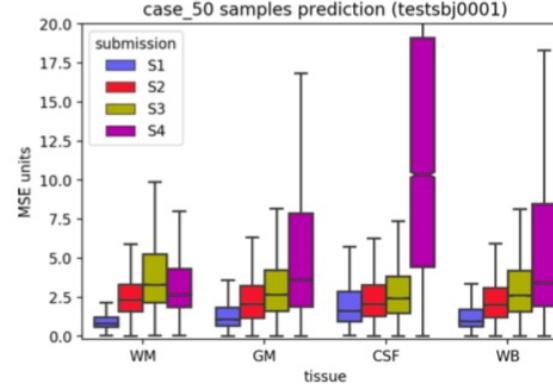
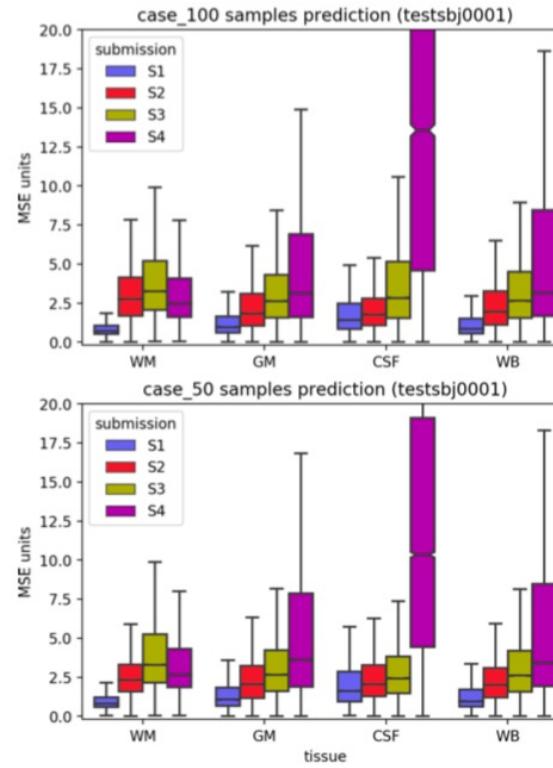
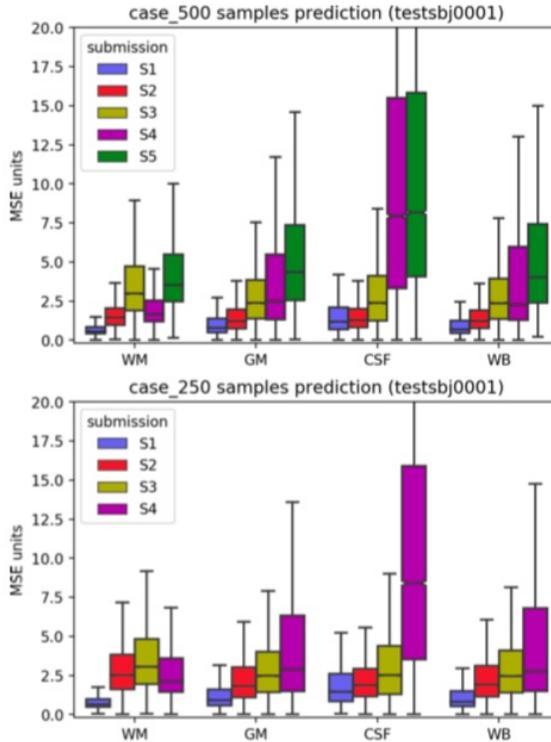


- SARDU-Net was used in the **2019 MICCAI MUDI Challenge** [8]
 - 1344 EPI volumes with variable (b , g ,TI,TE) provided for 5 subjects
 - participants ask for subsets of 50, 100, 250, 500 measurements in 3 subjects
 - participants predict the full set of 1344 measurements in those 3 subjects

qMRI upsampling: MUDI (1)



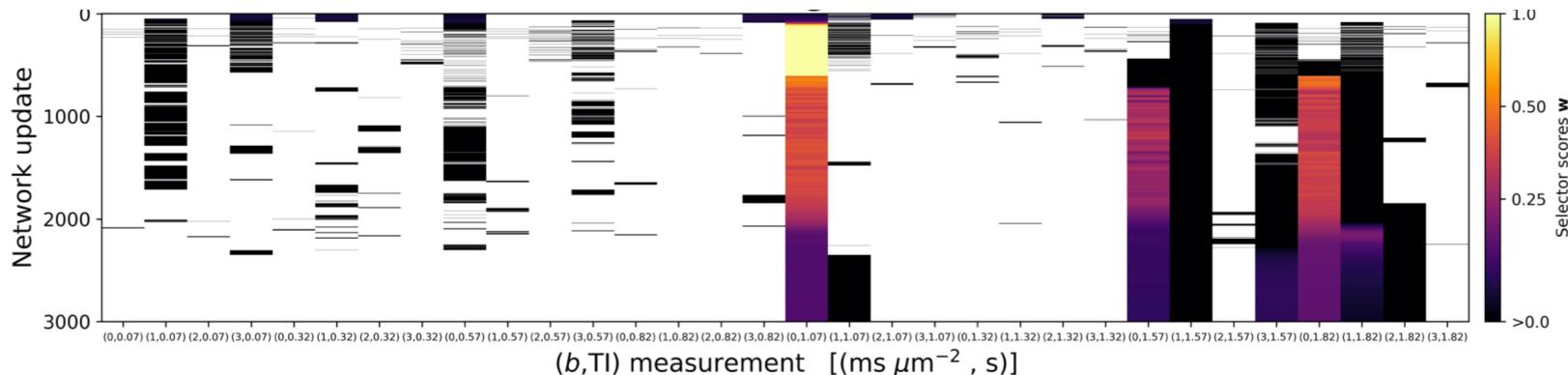
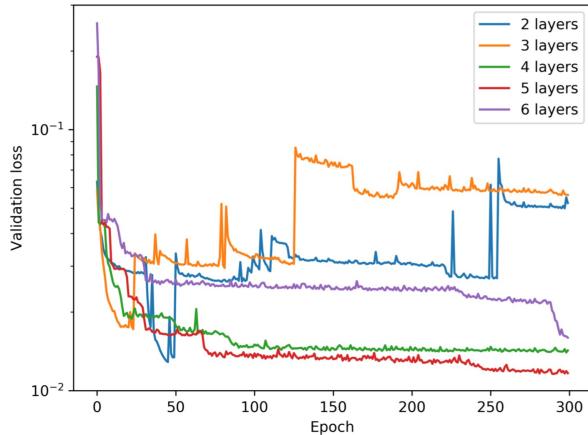
qMRI upsampling: MUDI (2)



- Ranked 1st on the Challenge Day at MICCAI 2019
- Ranked 2nd when the Challenge was reopened until Spring 2020

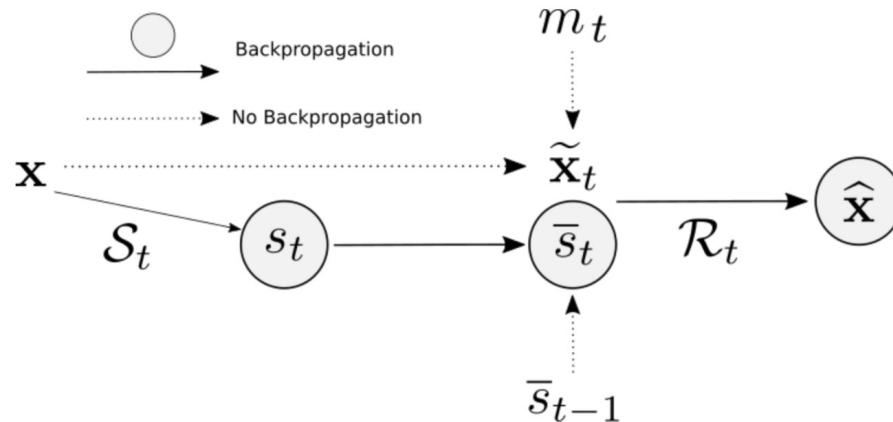
Methodological consideration

- SARDU-Net is promising but ...
 - *training stability could be improved*
 - *which architecture is best?*
 - *can we avoid **hard** thresholding?*



The PROSUB framework

Progressive Subsampling for Oversampled Data (PROSUB)



Outer loop

- Network Architecture Search (NAS)

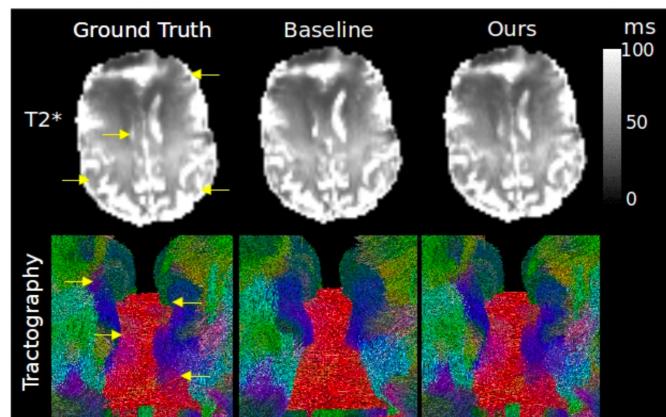
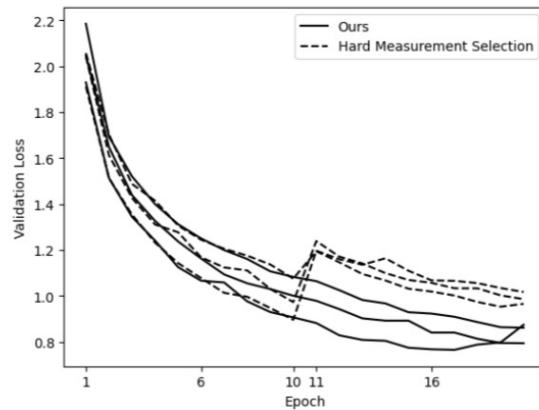
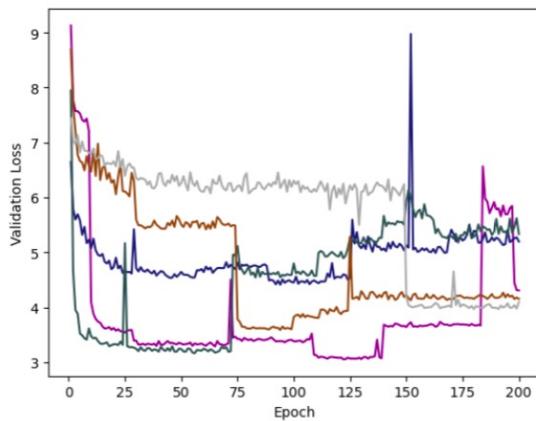
Inner loop

- Progressive construction of the measurement subset (recursive feature elimination)
- Measurements are scored iteratively (scored at iteration t depends on score at $t - 1$)

PROSUB performance (1)

As compared to SARDU-Net, PROSUB achieves:

- *more stable and more informative sub-protocols*



PROSUB performance (2)

As compared to SARDU-Net, PROSUB achieves:

- *more stable and more informative sub-protocols*
- *more accurate predictions of fully sampled signals*

		MUDI Challenge M for $N = 1344$				
		500	250	100	50	
SARDU-Net-v1	[14,26]	Baseline	1.45 ± 0.14	1.72 ± 0.15	4.73 ± 0.57	5.15 ± 0.63
SARDU-Net-v2	[4,15]	Baseline	0.88 ± 0.10	0.89 ± 0.01	1.36 ± 0.14	1.66 ± 0.10
SARDU-Net-v2-BOF	[4,15]	Baseline	0.83 ± 0.10	0.86 ± 0.10	1.30 ± 0.12	1.67 ± 0.12
SARDU-Net-v2-NAS		Baseline	0.82 ± 0.13	0.99 ± 0.12	1.34 ± 0.26	1.76 ± 0.24
PROSUB w/o NAS		Ours	0.66 ± 0.08	0.67 ± 0.09	0.88 ± 0.07	1.54 ± 0.11
PROSUB		Ours	0.49 ± 0.07	0.61 ± 0.11	0.89 ± 0.11	1.35 ± 0.11

Discussion and conclusions



- Data-driven, model-free protocol design: alternative to model-based optimisation
 - *may be useful when the model to use is not known*
 - *may be useful to shorten protocols in clinical studies if need arises*
 - **do NOT replace model-based optimisation**

Discussion and conclusions



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- SARDU-Net and its extension PROSUB are tools for model-free protocol design
 - *find out which measurements are informative*
 - *potentially “enhance” a qMRI protocol*

Discussion and conclusions



- Data-driven, model-free protocol design: alternative to model-based optimisation
 - *may be useful when the model to use is not known*
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 - *do NOT replace model-based optimisation*
- SARDU-Net and its extension PROSUB are tools for model-free protocol design
 - *find out which measurements are informative*
 - *potentially “enhance” a qMRI protocol*
- Future work will
 - *extend the method to convolutional architectures*
 - *test its utility beyond imaging*

Acknowledgments



Feasibility of Data-Driven, Model-Free Quantitative MRI Protocol Design: Application to Brain and Prostate Diffusion-Relaxation Imaging



Francesco Grussu^{1,2,3}, Stefano B. Blumberg², Marco Battiston¹, Lebina S. Kakkar⁴, Hongxiang Lin², Andrada Ianuş⁵, Torben Schneider^{6,7}, Saurabh Singh⁴, Roger Bourne⁸, Shonit Punwani⁴, David Atkinson⁴, Claudia A. M. Gandini Wheeler-Kingshott^{1,9,10}, Eleftheria Panagiotaki², Thomy Mertzanidou² and Daniel C. Alexander²*

Progressive Subsampling for Oversampled Data - Application to Quantitative MRI



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Acknowledgments



- **Thanks to Marco Palombo, Ting Gong, Gary Zhang for the invitation**
- Engineering and Physics Research Council (EPSRC EP/R006032/1)
- European Union Horizon 2020 programme (grant agreement 634541)
- Beatriu de Pinós Fellowship 2020 BP 00117, funded by the Secretary of Universities and Research (Government of Catalonia, Spain)
- “La Caixa” Foundation, Spain



"la Caixa" Foundation

