Physiological noise characteristics in fMRI of the rodent at 11.7T

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Introduction Temporal signal-to-noise ratio (*tSNR*) is the essential parameter for any BOLD fMRI protocol, as it limits the sensitivity to BOLD signal changes, whether they stem from stimulus-induced neuronal activity or from resting-state fluctuations. Thermal noise affects the tSNR as well as the single image SNR (SNR_0), but the limiting factor of tSNR may be of different origin: Physiological noise stemming from local T2* fluctuations may severely compromise the tSNR and linearly scales with the signal amplitude. According to the physiological noise model introduced by Krüger and Glover [1], the total noise consists of thermal noise σ_0 and the signal dependent physiological noise σ_p as descri bed by **Eq. (1)**. Thus, gains in SNR_0 above a certain level will no longer translate into an improved temporal SNR. This saturation effect between tSNR and SNR_0 is expressed in **Eq. (2)**. Animal imaging profitted immensely from higher field strengths and improved hardware, especially in the field of fMRI. The goal of this study is therefore to investigate the physiological noise characteristics in BOLD fMRI protocols of the rodent at a very high field strength of 11.7 Tesla. In particular, the individual contributions of thermal and physiological noise shall be determined using the physiological-to-thermal-noise ratio (PTNR) as defined in **Eq. (3)**.

$$\sigma = \sqrt{\sigma_0^2 + \sigma_p^2} = \sqrt{\sigma_0^2 + \lambda^2 S^2} \qquad (1)$$

$$tSNR = \frac{SNR_0}{\sqrt{1 + \lambda^2 SNR_0^2}} \qquad (2)$$

$$PTNR \equiv \frac{\sigma_p}{\sigma_0} \qquad (3)$$

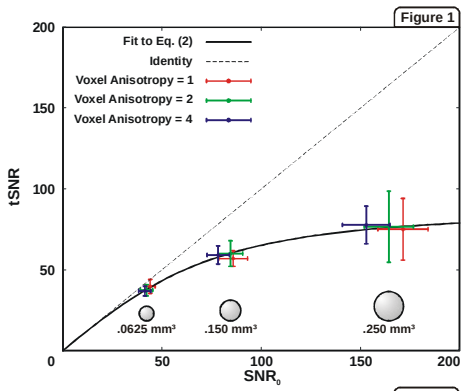
Table 1: Resolution and Voxel Geometry in EPI Protocols

No.	Resolution [µm]		Voxel Geometry	
	in-plane	slice	Vol. [mm³]	Aniso.
1	630 x 630	630	0.2500	1
2	500 x 500	1000	0.2500	2
3	397 x 397	1586	0.2500	4
4	500 x 500	500	0.1250	1
5	397 x 397	793	0.1250	2
6	315 x 315	1260	0.1250	4
7	397 x 397	397	0.0625	1
8	315 x 315	630	0.0625	2
9	250 x 250	1000	0.0625	4

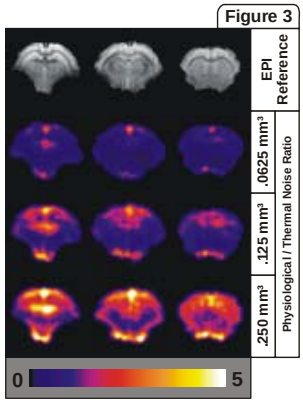
Methods Male Wistar rats (n=5, 300-400g) were anaesthetized using Isoflurane (1-2%) in a mixture of 30% O_2 and 70% N_2O. Respiration was monitored using a breathing pad, body temperature was feedback controlled and maintained at 37°C. Animals were fixed in the cradle using ear and bite bars and were positioned to align the magnet isocenter with the center of the brain. MRI was performed on a Bruker BioSpec 11.7 T with a maximum gradient amplitude of 750mT/m and minimum ramp time of 100µs using a 72mm quadrature resonator for transmission and a standard quadrature surface coil for signal reception (Bruker BioSpin, Germany). Time series of single-shot multislice gradient echo planar images (GE-EPI) each consisting of NR=64 repetitions were collected using TE=18.0 ms / TR=3000 ms / 64x64 matrix / bandwidth 150 kHz. Five coronal slices were obtained with a slice distance of 2.5mm to avoid slice crosstalk. To assess physiological noise, voxel volume was varied via in-plane resolution and slice thickness according to **Tab. 1**. Additional scans with zero flip angle were acquired to assess the thermal noise.

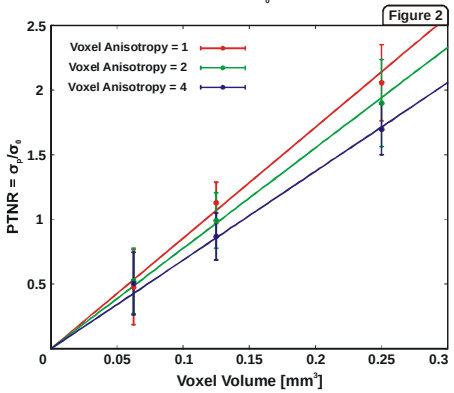
Analysis Prior to further processing, GE-EPI time series were motion corrected using FSL. From each time series, maps of the temporal mean and standard deviation (SD) where calculated on a pixel-by-pixel basis. Thermal noise level was estimated from the temporal standard deviation in the corresponding zero flip angle series multiplied by 1.527 to account for the Rayleigh distributed magnitude image [2]. Temporal mean and SD maps underwent an ROI based analysis using ImageJ. To minimize ROI dislocation errors arising from the various in-plane resolutions, the ROI was selected to cover the full brain in 3-4 center slices, sparing brain borders and regions prone to vascular fluctuations. Across the ROI, temporal mean and SD were reduced to single values. Additionally using the estimated thermal noise level, this allowed for calculation of image SNR (SNR_0) and temporal SNR (tSNR) across the brain for each time series. For the various resolutions, tSNR and SNR0 were averaged over the five animals and plotted to fit Eq. (2), determining the saturation parameter λ. The ratio of physiological to thermal noise (PTNR) was calculated according to Eq. 2.To visualize the spatial distribution of physiological noise, the PTNR was also calculated on a pixel-by-pixel basis for selected datasets, c reating PTNR maps.

Results **Fig. 1** illustrates the comparison of tSNR vs. SNR0 and clearly shows the expected saturation of the tSNR with increasing image SNR. A fit of these data to Eq. 2 yields a parameter of λ = 0.01176 (±1.6%), indicating saturation of the temporal SNR around tSNR→85. As depicted in **Fig. 2**, the contribution of physiological noise increases linearly with the voxel size, whereas thermal noise remains constant. Slight differences in this particular behaviour are noticeable as protocols are analyzed regarding their different voxel aniso-tropy: λ values increase towards more isotropic voxels, meaning that the tSNR saturates on a lower plateau compared to when anisotropic voxels are used. This behavior becomes more apparent in **Fig. 2**, where the physiological noise is shown to increase steeper with voxel size for isotropic voxels. **Fig. 3** is a showcase of PTNR maps for a set of EPI images acquired with identical in-plane resolution but varying slice thickness. It is again shown that physiological noise generally increases with the voxel size. Furthermore, physiological noise is especially prominent in the proximity of larger vessels and ventricles and appears to be more pronounced in the cortex compared to subcortical structures.



Discussion The preliminary results of this study confirm the general model for physiological noise [1] in translation to BOLD fMRI protocols of the rodent at a very high field strength of 11.7T. Increasing the image SNR by modulating the voxel size lead to the expected saturation behaviour of the temporal SNR. The characteristics of this saturation - as described by the parameter λ – are in line with results from human studies [3]. It turns out that typical fMRI protocols for the rodent at 11.7 Tesla may contain considerable contributions of physiological noise comparable to or exceeding the thermal noise level. The presence of physiological noise in fMRI time series may compromise the temporal SNR on the one hand; on the other it indicates a certain sensitivity to physiological fluctuations, which is of great importance e.g. in resting state fMRI. The ratio of physiological to thermal noise may be an important indicator to optimize MRI protocols for a specific application [4]. As the origin of physiological noise is still not fully understood, further investigations should address the separation of BOLD-like and non-BOLD components of physiological noise [1,2]. Furthermore, the various anaesthesia protocols used in fMRI of the rodent may generate different baseline conditions regarding blood flow and neuronal activity, which could be of importance for physiological noise and needs further investigation.





Literature [1] Krüger and Glover (2001), MRM 46:631-7 [2] Gudbjartsson and Patz (1996), MRM 34:910-4 [3] Triantafyllou et al. (2005), NeuroImage 26:243-50 [4] Bodurka et al. (2007), NeuroImage 34:542-9