fMRI User Guide

Electrophysiology recording during functional MRI

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fMRI User Guide

Electrophyisology Recording in Functional MRI (fMRI) Environments using TDT

This document is a hardware and software instructional reference for conducting electrophysiology recordings in Functional MRI (fMRI) environments using TDT hardware and software.

The challenge of using both modalities simultaneously is that the electrophysiology recording system can introduce imaging artifacts, and the MRI system introduces artifacts on the electrophysiology system. The purpose of this guide is to discuss proper hardware/software setup to minimize these artifacts.

This guide will not go into any meaningful details about electrode placement or implantation surgery, and assumes you can record clean signals outside of the fMRI environment.

Motivation

Electrophysiology and fMRI are two very different types of recording modalities. The first is recording electrical activity from the brain of a subject. The data is filtered for both fast neural/spiking activity and longer term activity of local field potentials (LFP). The subject can be head-fixed or freely moving.

In fMRI the subject is head-fixed and restrained in a tube. It measures changes in blood flow and relies on the fact that blood flow and neuronal activity are coupled. The activity is on a longer time scale, from several seconds to minutes. This looks at the whole brain as opposed to a very small section of the brain.

Combining the two recording methodologies provides a better understanding of the underlying architecture of the brain. You can use the electrophysiology to validate the fMRI data by determining a correlation between fMRI signals and LFP or spiking data. You can also record both neural activity and fMRI activity from multiple sites to see time course of signals in the brain.

You can use the electrophysiology data to validate the blood-oxygen-level dependent (BOLD) signal in fMRI. Integrating the two helps you understand the relationship between BOLD and

neural responses to stimulus, and elucidate the underlying neural activity driving the BOLD response.

Getting Started

Hardware Requirements

One of the challenges of recording electrophysiology during fMRI is the large artifact introduced by the scanner during imaging. The scanner artifact can be >100 mV on the recording signal, so you need a headstage and amplifier that won't saturate (clip) during the scan.

Headstages and Electrodes

Only non-ferrous headstages (passive or active) and electrodes should be used in the fMRI to avoid image distortion. See Minimizing Imaging Artifacts for an example of the image distortion

TDT non-ferrous headstages are available in 16-channel (LP16CH-ZNF) and 32-channel (LP32CH-ZNF) form factors, with standard 2 m cable. These headstages have a ±2.5 V input range, unity gain, and no filters.



For single unit / LFP recording, only fMRI-compatible probes can be used, with sites made of Platinum-Iridium (PtIr) or other materials. For EEG / EMG use non-ferrous materials that are also generally biocompatible. Some suggestions for material might be titanium (perhaps good for skull screws), Ag/AgCl, or gold. Make sure you also have non-ferrous wiring going out of

the electrodes to whatever downstream headstage or connector you are using. Copper, gold, or platinum wires could work. Gold and platinum might be expensive though, and copper wire may heat up some during the scan.

Amplifier

Both the PZ5 analog amplifier and PZA Subject Interface (SI) analog amplifiers have a large enough input range (±500 mV) that they can handle artifacts from the scanner without saturating. They also have a large 124 dB dynamic range (least significant signal ~100 nV) to precisely capture the electrophysiology signal and can be DC-coupled to minimize signal distortion.

These are the only amplifiers that should be used with fMRI. Other amplifiers, including the digital headstages, have a much smaller input range and built-in filters. High-pass filters cause temporal shifts that make it more difficult for artifact removal. Low-pass filters cause ringing after the scan which increases the amount of signal lost immediately after the scan.

MRI Kit

TDT provides two cable kits for MRI compatible connections between the subject electrode interface and the amplifier, one for 16 channel headstage connections and one for 32 channel configurations.



The standard non-ferrous headstage cable is two meters. The MRI kit includes a two meter extension cable, so the distance between the amplifier and subject can be extended to four meters. This overall length is typically sufficient, but if more length is required then additional one meter extender cables are available. This length is measured from the center of the bore to the waveguide / filter plate interface between the MRI room and the control room.

The MRI-NRKIT-16, 16 channel kit includes:

• (1) PassThru, passive extender cable, two meter length

- (1) PA-DB25F, DB26 male to DB25 female connector
- (1) PA-DB25M, DB26 female to DB25 male connector
- (1) RFFILT-3M, RF filter with 50 MHz low pass

The MRI-NRKIT-32, 32 channel kit includes:

- (2) PassThru
- (2) PA-DB25F
- (2) PA-DB25M
- (2) RFFILT-3M

See Penetration Panel for a discussion on the RF filter.

Each kit includes a 50 kOhm resistor test block for your headstage type (16-channel or 32-channel Omnetics).



MRI test resistor blocks

Omnetics-Omnetics connectors (pin savers, gender change, or angled connectors) for connecting in tight spaces are available on request.

RZ Processor

The PZ5 and PZA Subject Interface connect to an RZ Processor. This handles the real-time signal processing, and communicates with the PC through an interface card.

Interface Card

The RZ Processor connects to the PC through either a PO5e or UZ3 PC interface.

Hardware and Software Setup

Carefully unbox your equipment and install the PO5e or UZ3 according to the System 3 Installation Guide. If you have a TDT WS4 or WS8 workstation, then a PO5e card will already be installed. Briefly - power down your computer* and place the PO5e card into an available PCIe slot in your computer. Next, install your TDT drivers and Synapse software from the USB Storage Drive that was provided with your shipment.



*TDT drivers only function on Windows machines. Synapse will not run on Mac or Linux.

Below is a list of helpful online TDT resources with which users should be familiar before starting:

Synapse Training Videos

Narrated walkthroughs of the Synapse software. These are very helpful for beginner users first learning the Synapse environment.

Lightning Videos

Short, unnarrated videos that demonstrate specific actions in TDT software. These are referenced several times throughout this document, so look out for the blue icon

Knowledge Hub

Contains documentation for all TDT hardware and software. This is a great first resource for troubleshooting

Tech Notes

Contain information about known hardware or software issues and associated solutions or workarounds

Support Help

TDT Tech Support offers phone and remote screen sharing support via GoToAssist to customers M - F, 8 AM - 5 PM Eastern Time. For remote screen sharing assistance, please email support@tdt.com to schedule an appointment.

Establishing RZ processor and PC communication

Once the PO5e card is seated and TDT drivers and software are installed, you are ready to connect the RZ processor and PC together. The orange fiber optic cables* will be used for PC-RZ communication (see Sys III manual for more details). Please connect the fiber optics to the correct ports on the RZ and PO5e card, as shown in the diagram below (red optical connector to 'Out' or Red-labelled ports on RZ and PC).



*Your fiber optic cable may be a different length.

PC-RZ communication







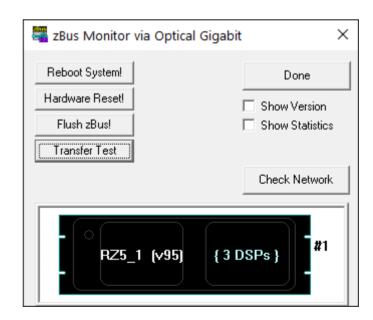
RZ



PC PO5e

Next, turn the RZ on. The display screen on the processor should illuminate with information about the unit's DSP cards. To check whether there is communication between the RZ and the PC, open the zBusMon application (shown to the right). The RZ processor should appear with information about the driver version and number of DSP cards. Click *Transfer Test* to test communication.

If you get an error upon performing an initial transfer test, try performing a 'Reboot System!' first. If there is a consistent error in zBusMon, or you do not see your RZ appear, please contact TDT for assistance.



zBusMon with RZ5D Processor

Connect your amplifier

- If using a PZ5 and RZ2 processor, connect the PZ5 to the port labeled **PZ Amplifier** on the back of the RZ2.
- If using a PZ5 and a different processor, connect it to the port labeled **To PZ**. On an RZ5D, this might be on the front panel. Otherwise it will be on the back of the RZ.
- If using a PZA Subject Interface, connect it to the optic port labeled To SI. On an RZ5D, this might be on the front panel. Otherwise it will be on the back of the RZ.



Important

The PZ5 and PZA Subject Interface are battery power and optically isolated. Make sure that the charger cable is disconnected from the amplifier and the wall sock while recording.

Launching Synapse

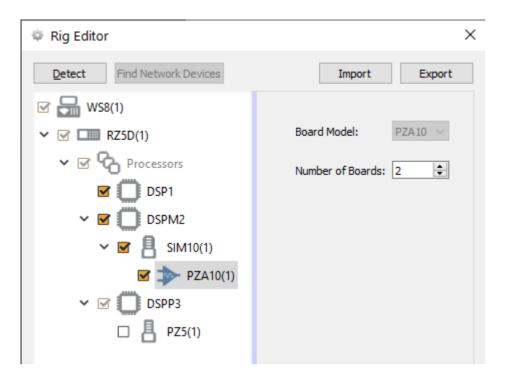
With your RZ and amplifier on and connected, launch Synapse. If this is your first time launching Synapse, the Rig Editor will appear and it will be blank. Click Detect for Synapse to recognize your RZ and the number of cards installed in your PZ5 or PZA Subject Interface, and their type.



Note

PZ5 card detection is available in v96 Synapse and later only.

In this example, a PZA Subject Interface is connected to an RZ5D. A PC, RZ5D, three DSPs, the Subject Interface (SIM10), and an unchecked PZ5 in the tree. Finally, click Ok to exit the Rig Editor.



The PZ5 is unchecked because there isn't one connected.



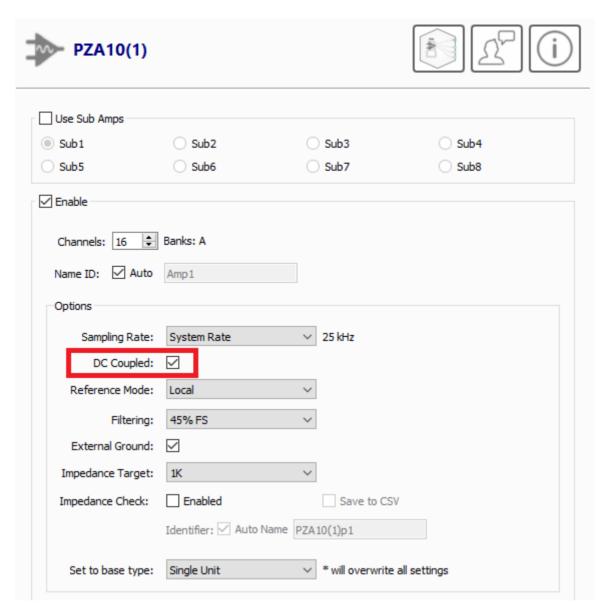
The Dig Editor can be accessed later for modification through the Synapse Me

The Rig Editor can be accessed later for modification through the Synapse Menu if your hardware changes.

Amplifier Setup

Software Configuration

In Synapse, in the PZ5 or PZA Subject Interface options set the subamplifier to 'DC Coupled' mode. Using DC coupling increases the probability that the artifact removal will be successful and avoids additional signal distortion caused by AC coupling.

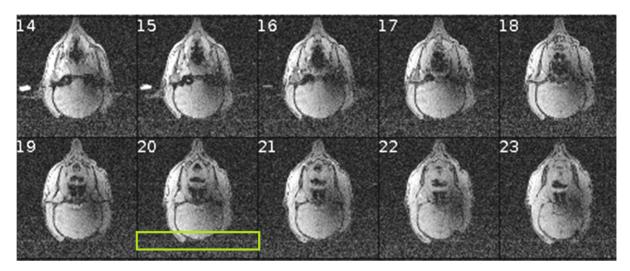


PZA configuration options

The External Ground option connects the subamplifier / subject ground to the banana jack on the back of the PZ5 / PZA Subject Interface. Note that the subject ground should never be connected to the MRI ground. See System Grounding section for more information on system grounding.

Touchscreen Configuration

The amplifier produces high frequency EMF that is outside of any electrophysiological signal range, but is in the frequency range used by the scanner. This can introduce noise artifacts in the scanner image, as shown in the example below. These artifact show up as faint white lines across the image.



Example amplifier artifact in scanner image

Two of the built-in features of the PZ5 / PZA Subject Interface introduce artifact and must be disabled during recording.

1. Turn off amplifier wifi

Older amplifiers have built-in wifi to allow network updates. This must be disabled during the scan (and can remain permanently disabled, use the Ethernet port to do network updates).

- PZ5: Press the 'PZ5' icon on the touchscreen -> Config -> More -> set Wireless to 'Off'
- PZA Subject Interface: Press the 'SIM' icon on the touchscreen -> Config -> set Wireless to 'Off'

2. Turn off amplifier touchscreen

The touchscreen is a big source of high frequency EMF. During the actual scan, the touchscreen must be turned off.

PZ5: Press the 'PZ5' icon on the touchscreen -> Config -> set 'Autosleep' to '5 min'. This
is currently the minimum setting and will turn off the touchscreen display after 5
minutes of inactivity.

To immediately turn off the PZ5 screen, make sure you are on the main screen and swipe three fingers across the screen in any direction.

• PZA Subject Interface: Press the brightness icon on the touchscreen, this turns off the touchscreen display after 5 seconds.



MRI Recording Processor Gizmo

Real-time Artifact Rejection

The MRI Recording Processor gizmo is built into Synapse software. It provides a series of tools for thresholding and removing MRI scanner artifact in single unit and LFP data in real-time during the MRI recording. The MRI Recording Processor gizmo drops in between your signal source and any spike sorting or LFP gizmos.

The gizmo:

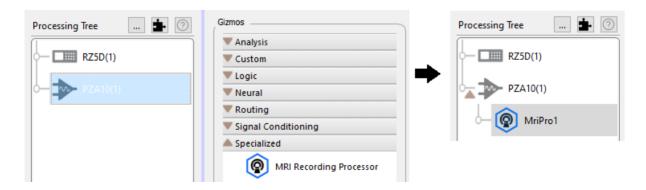
- Has adjustable threshold and rejection windows for automatic detection and removal of artifacts in the electrophysiological data stream
- Saves the raw data for offline analysis and artifact subtraction
- Has special filters that reduce ringing after the artifact blanking period has passed, tuned specifically for single unit and local field potential (LFP) signal ranges
- · Visualization of neural activity (single unit and LFPs) with and without artifact

The rejection window can be triggered automatically when an artifact is detected or by an external logic signal that syncs to the MRI scanner switching.

See the Synapse Manual for more information.

Configuring the Gizmo

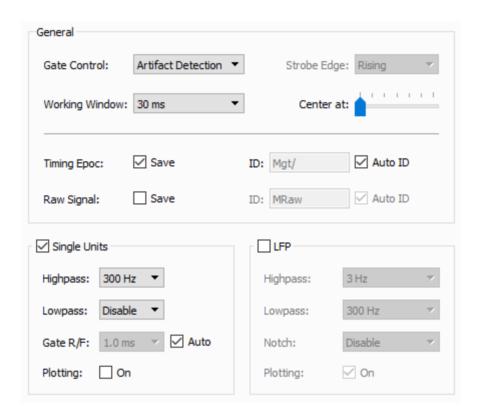
Select the PZ5 or PZA object in the Processing Tree and find the MRI Recording Processor gizmo in the Gizmos list. Drag and drop, or double-click, the gizmo onto the PZ5 / PZA to form a connection.





You can learn more about gizmos and experimental connections in the Synapse Manual.

The MRI Recording Processor has several configuration options for managing how the artifact is detected and gated, and for which type of filtered waveform is output for other downstream processes. In this configuration, a threshold crossing is used to trigger the artifact rejection.



MRI gizmo options for threshold crossing

Working Window determines how much of the signal to view when an artifact is triggered. Make sure this window is long enough to capture the entire artifact you want to remove.

Optionally save the Timing Epoc to get timestamps when artifacts are detected, stored synchronously with your data as the default epoc event "Mgt/".

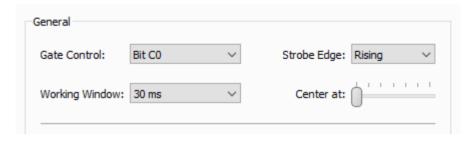
You can save the raw signal for offline analysis and artifact subtraction. You can also filter/visualize for Single Unit and/or Local Field Potentials frequency ranges.

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Important

Enabling **Plotting** for Single Unit/LFP shows you the signals from all channels in the flow plot, but does not save the data. Storage gizmos, such as the Stream Data Storage, must be attached to the gizmo output link for saving. Be sure to set the sampling rate appropriately for the bandwidth of data you are trying to capture.

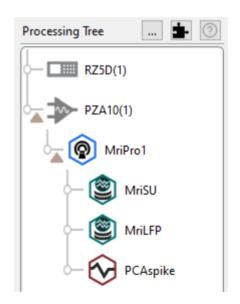
If the MRI has a digital signal that triggers during the scan, this can be connected to the RZ front panel digital input and used to trigger the artifact rejection.



MRI gizmo options for digital input trigger

Synapse Experiment Setup

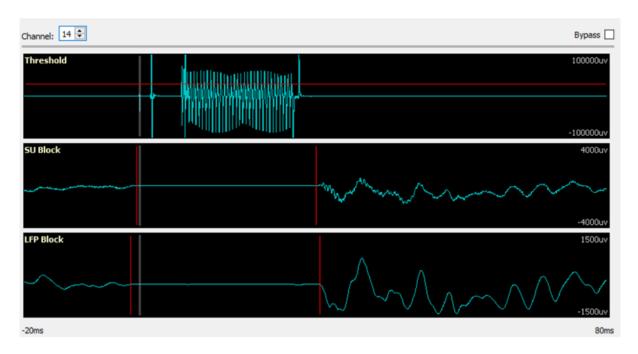
A typical MRI recording setup would look like this. The PZA Subject Interface or PZ5 amplifier routes raw recording signals to the MRI gizmo for processing and filtering. The outputs for Single Unit and LFP filter signals are saved in Stream Store Processors at the appropriate sampling rates. If the MRI has a digital Sync line to mark magnet switching, then a bit input would also be configured in the RZ.



A common processing tree for an MRI recording experiment

Example Run-Time View

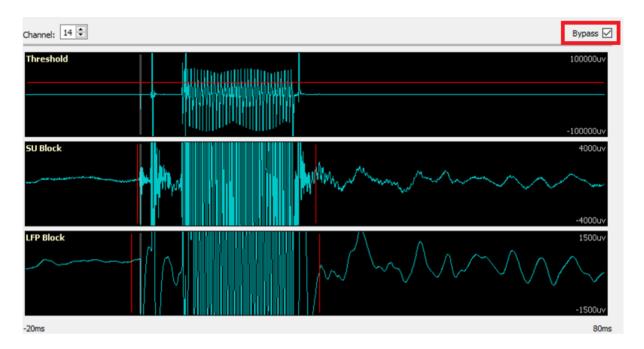
The MRI tab at run-time has the raw signal visualization and selected Single Unit and/or LFP plots. The amount of data is shows is set by the Working Window option during Idle. The gray vertical bar is the start of the artifact. Its location is set with the 'Center At' option.



- 1. Select a channel with a good representative artifact.
- 2. Set the artifact rejection threshold in the top plot by click-dragging the red bar. If you don't see the bar, it is outside the current window view. Right-click on the plot and select 'Find Threshold'.
- 3. Set the bounds of your artifact removal window in the Single Unit and LFP plots by click-dragging the vertical red bars. Single Unit and LFP data are handled differently, due to the different frequency characteristics of these signals, to minimize signal ringing at the end of the removal window.
- 4. Check that the rejection window works on all channels. There is significant variation in the amplitude of the artifact from channel to channel and also from scan to scan.

Thresholding and filter widths for each signal type can be adjusted during runtime. A threshold crossing on the channel you are viewing is used to trigger the same rejection window on all channels at exactly the same time. If you change the channel, the threshold bar and window stays in the same spot, but now the rejection happens when this new channel crosses the threshold.

You can also bypass the rejection to see the full scanner artifact and signal. This can help in setting up the appropriate rejection window and validating the artifact removal. Check **Bypass** on the upper right corner of the run-time interface.



Physical Setup and Testing

The headstage cable should be aligned with the center of the bore and extend straight out from the isocenter of the magnet. Make sure the headstage cable is long enough for this.

The amplifier may generate artifacts on the scan if inside the MRI room. Set the amplifier as far away from the scanner as possible. Placing it outside the 5 gauss line is best, if possible. Leaving the amplifier in a strong magnetic field will either cause the batteries to fail or shorten the battery life of the amplifier.



Danger

Connectors on the PZ5 / PZA Subject Interface are ferrous and will be attracted to the magnet. Use extreme caution when handling the amplifier anywhere near the magnet. In general the PZ5 / PZA Subject Interface is heavy enough it won't be pulled into the bore, but it should remain outside the 5 gauss line if possible.

Penetration Panel

The scanner room is well-shielded against radio frequency (RF) noise that affects the image quality. The headstage cable passes from the scanner room to the control room through a penetration panel that may contain RF filters and waveguides.

Penetration panels limit the high frequency signals emitted by the PZ5 / PZA Subject Interface amp. They do not resolve RF noise that is generated along the cable from the PZ5 / PZA Subject Interface amp to the MRI. Any additional RF noise can be filtered with the passive lowpass 50 MHz RF filter that comes with the TDT MRI-KIT. The RF filter is placed in-line between the amplifier and headstage. All wires (recording channels, subject ground, and reference) pass through this filter. This has to be grounded properly to work*. It has standard 1.5 mm DIN (touch-proof) connectors to connect to the ground on the scanner itself. This then connects to the RZ processor for real-time scanner artifact removal.



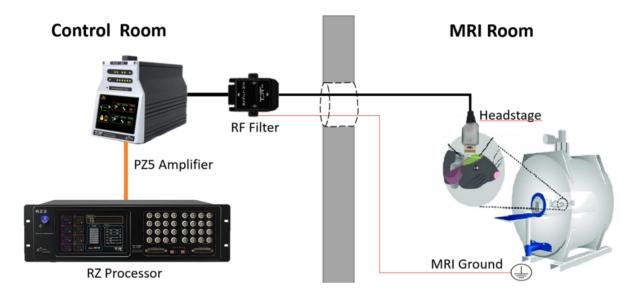
Important

*The RF filter ground is different than the subject ground.

The penetration panel and RF filter do not remove scanner artifact from the neural recordings. This is done on the RZ processor in real-time using the MRI Recording Processor gizmo, as discussed in the MRI Gizmo section.

Waveguide

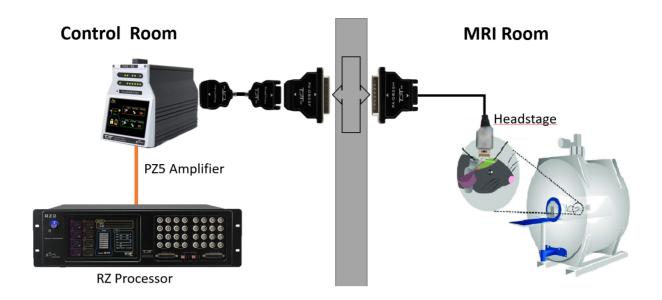
Waveguides are tubes that are a part of the penetration panel. The headstage cables simply pass through. The non-ferrous MRI-compatible headstage is connected to the MRI-compatible electrode. This goes through a very long cable (up to 6-7 m) to the control room to the PZ5 / PZA Subject Interface. Know the length from the bore isocenter to the waveguide when determining what length of cable is needed. The full setup looks like this:



Filter plate

In addition to the waveguide, there is also often a filter plate for BNC and DB25 connectors on the penetration panel to pass signals between the MRI room and the control room. Use the DB25-female and DB25-male connectors provided in the TDT MRI kit to connect the headstage through the filter plate to the amplifier.

Some filter plates are just pass-through connections, in which case you need to use the TDT RF filter in the cable connection.



Minimizing Amplifier Artifact During MRI Scans

We recommend the following setup:

- 1. Place the PZ5 / PZA Subject Interface amplifier outside the MRI room in the control room or component room. You can place the amplifier on a cart in the control room just outside the penetration panel. All cables pass through either a waveguide on the penetration panel or through a DB25 connector on the panel.
- 2. Turn off the wifi and the front display screen on the PZ5 / PZA Subject Interface amplifier. See Touchscreen Configuration.
- 3. Test the system using a phantom with no RF filter. This is your baseline signal.
- 4. If there is significant artifact connect the RF filter to the back of the PZ5 / PZA Subject Interface amplifier and the GND on the RF filter to either:
 - a. The MRI GND. This is the GND found on the gradient power supply. This GND is floating relative to earth and will remove most of the artifact.
 - b. Room or Shield GND. This is the GND found in the penetration panel, which is connected to the shielded room around the MRI. This shield usually goes to truth earth GND. This will remove some but not all the artifact.
- 5. PZ5/PZA configuration a. Disable External Ground b. Run the PZ5/PZA at 50 kHz if possible. Adjust the RZ processor sampling rate to 50 kHz as well. c. DC couple

Large Scanner Setups

Scanners designed for humans and used for non-human primate (NHP) and large animals (pigs) are normally 3T and 7T large bore scanners. Large scanners are enclosed and do not have direct access to the MRI GND. Engineers are averse to providing access to GND lines that are accessible from the power and control room.

Small Scanners

Scanners designed for small NHP and rodents. These scanners are high field scanners designed for specialized measurements in rodent, small mammal and small NHP such as marmosets. They range in power from 4.7 to 16.8 T and the bore diameter is on the order of a 10-20 centimeters. These scanners will often have built in shields and may have easy access to the MRI GND. The GND should be on the MRI or in the gradient supply in the nearby component room.

Vertical Scanners

Some NHP groups have vertical Brukner 4.7 and 9.4 T scanners. These scanners present a significant problem when attempting to place the PZ5 / PZA Subject Interface amplifier at a distance from the scanner. In this case the preamp should be as far away from the gauss field of the magnetic (>50 gauss). If possible, connect the GND of the MRI to the GND on the RF filter.

Testing

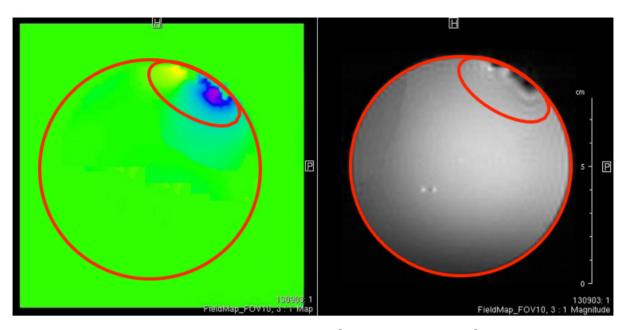
Minimizing Imaging Artifacts

The first step is to verify that the neural recording system introduces minimal image artifact.

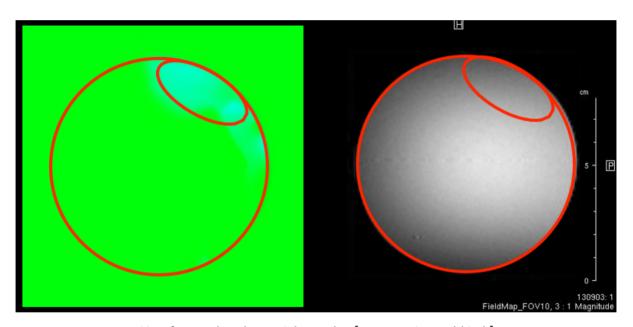
To do this:

1. Setup an agar gel or saline phantom with the headstage and electrodes to image the baseline noise. Verify RF noise is minimal and there is no field distortion.

Example field maps (measure of signal distortion) and real images for ferrous and non-ferrous headstage/electrodes are shown below.



Ferrous headstage/electrodes [courtesy Leopold Lab]



Non-ferrous headstage/electrodes [courtesy Leopold Lab]

Scanner Artifacts in Neural Recording

The next step is to verify the integrity of the neural recordings, both before and during the scan. The scanner artifact can be >100 mV on the recording signal. MRI artifact is not correlated with the field size. The bore diameter will have a bigger effect.

To do this:

- 1. Perform test recordings with the 50 kOhm resistor block in the fMRI kit. This tests the integrity of the headstage / amplifier recording as a baseline.
- 2. Run the system without a scan to observe the baseline noise.

- $_{
 m 3.}$ Run the system with a scan to view the scanner artifact on the neural recording. Look for any saturation, and use the MRI Recording Processor gizmo interface to remove the scanner artifact.
- 4. View the scan to determine if there are any image artifacts.

Repeat the above tests in steps 2-4 with your electrode using an agar gel or saline brain phantom for a complete system test, from electrode to amplifier.



Important

With electrode in subject, check the neural recording data quality on the table top before moving it into the magnet. If there are issues, perform a standard saline test outside of the magnet as well.

Troubleshooting FAQ

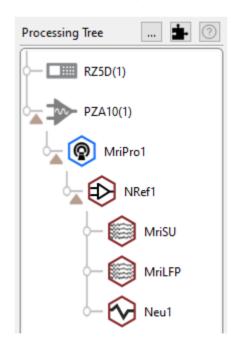


Ringing still present

Depending on the scanner artifact there could still be ringing in the Single Unit / LFP filters of the MRI Recording Processor gizmo after the artifact window has passed. In this case, only enable the Single Units artifact rejection and disable the built-in filters.



Add a Neural Signal Referencer gizmo to further clean up signal after the MRI Processing gizmo, then filter and store with Neural Stream Processor gizmos. The Processing Tree looks like this:



Note that this will work only for electrodes close to each other as the scanner artifact varies significantly between electrode channels.

2

Noise through filter plate

If your MRI setup has a filter plate separating the control room and MRI room, the filter plate may have additional RF filtering. Sometimes the filter plate may slightly increase noise in the image. In that case, use a waveguide if available and the TDT RF filter.

2

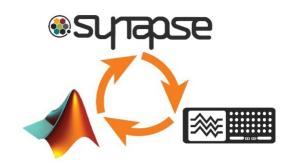
Using the PZ5 / PZA Subject Interface in the MRI room

If the distance from the scanner room to the control room is >5 meters (e.g. vertical bore magnets such as the Brukner 9.4 T) it may be necessary to leave the PZ5 / PZA in the MRI room. In that case the further the PZ is from the peak gradient lines the longer the battery life. We recommend that the guass field be less than 50 guass

Post Processing & Data Analysis

TDTbin2mat and the MATLAB SDK

Exporting data from Synapse into MATLAB is simple with the TDT MATLAB SDK. The main importing function of the MATLAB SDK is TDTbin2mat. The main argument for TDTbin2mat is the full file path to the data block that you want to import. Synapse makes copying this file path easy via the History dialog. See the *Lightning Video* to see this importing sequence.



You can also copy the block file path via Windows Explorer.



https://www.tdt.com/docs/lightning/synapse/#importing-into-matlab

Link to the MATLAB SDK: https://www.tdt.com/docs/sdk/offline-data-analysis/offline-data-matlab/getting-started/

The TDT Python Package

Data can also be easily imported into Python 3 using the tdt package. If you already have Python 3 installed, you can add the tdt package in your cmd window: pip install tdt



Link to Python Package and SDK:

https://pypi.org/project/tdt/

https://www.tdt.com/docs/sdk/offline-data-analysis/offline-data-python/getting-started/

Release notes and select examples

MATLAB and Python Workbook Examples

TDT aims to help customers as much as possible with easy data import and analysis. We understand that not all customers have extensive MATLAB or Python experience, so we created fully-commented workbook examples that demonstrate how to do basic, but interesting operations with MATLAB or Python code. These examples are not intended to serve as a complete pipeline for your data analysis - please use wisely.

Link to MATLAB Workbook examples

Link to Python Workbook examples

If you have other scripting needs, please reach out to TDT Tech Support at support@tdt.com.

View Data in OpenScope

For a first-pass replay of data, you can view any Synapse recording in OpenScope. This also takes advantage of the Synapse History dialog. OpenScope has extra features that make jumping around the data fast and intuitive. You can also use the Video Viewer feature to replay videos with the timestamp of each frame.

Using OpenScope



https://www.tdt.com/lightning/#ViewDataInScope



https://www.tdt.com/lightning/#VideoViewerScope