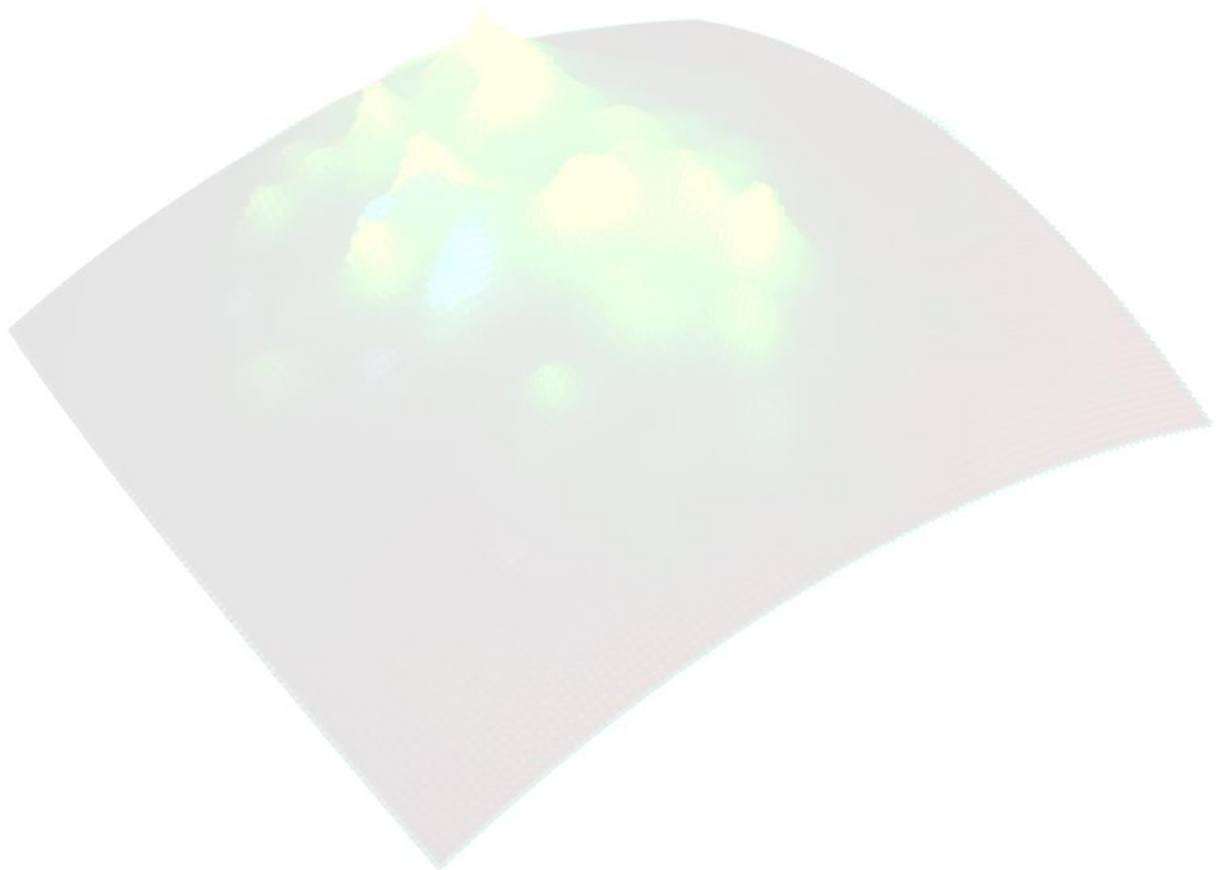


# TMSmap<sup>®</sup>

Software for transcranial magnetic stimulation data analysis

Version 1.9.1.ob

## User Manual



April 2019

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## 1 About the software

TMSmap software (<http://tmsmap.ru/>) is developed as a standalone graphical interface software for the quantitative analysis of the results of transcranial magnetic stimulation (TMS) mapping. The software allows to consider not only standard parameters like the size of the cortical muscle representation and hotspot and center of gravity (CoG) location, but as well the volume of the representation considering the amplitude of MEPs in each stimulation spot, the shape of the area, the profile/landscape of the muscle cortical representation and the overlap between representations. Earth mover's distance (EMD) metric is implemented into the software for maps profiles comparison. Please see the open access article [Novikov et al., 2018](#) (doi: 10.3389/fnhum.2018.00239) for more details.

The software was written using WPF (C# and XAML). One can download, install and use it free of charge. Please cite [Novikov et al., 2018](#) (doi: 10.3389/fnhum.2018.00239) article if you use this software.

## 2 Video tutorial

One can find video tutorial materials:

- Brief version (duration: 5 minutes) is available by the link <https://www.youtube.com/watch?v=WvwEnw0wGGE&t=4s>;
- Detailed version (duration: 18 minutes) is available by the link <https://www.youtube.com/watch?v=sWm0G-G-614>.

## 3 System requirements

- Microsoft® Windows® 7 or higher;
- Microsoft® .NET Framework 4.6.1 or higher (if this component is missing on the system, one can download it here <http://www.microsoft.com/downloads>).

## 4 Used packages

- ClosedXML (<https://github.com/ClosedXML/ClosedXML>) is used to generate output files in .xlsx format;
- Implementation of the Earth mover's distance (EMD) metric is based on the modification of the open-source C++ code which was available by the link <http://ai.stanford.edu/~rubner/emd/default.htm#LOG>.

## 5 License

The software is distributed under a freeware license. There is detailed information about the license in the **license.txt** file of the downloading package of the TMSmap as well as in

the **Info->License** of the main menu of the software. Briefly, one can download, install and use it **free of charge**. Please cite [Novikov et al., 2018](#) (doi: 10.3389/fnhum.2018.00239) article if you use TMSmap software.

## 6 Download

Files downloading is available after the registration on the website <http://tmsmap.ru/>. Please choose **Download** section, below the section you could see software' versions, user manual and exemplary data. It is recommended to download the latest version of the software.

After downloading one can extract software and exemplary data files from the .zip or .7z archives. So, one can see **TMSmap\_v...** folder, **Example\_data...** folder and user manual pdf-file.

## 7 Start

Double click on the **tmsmap.exe** file in the **TMSmap\_v...** folder to start the application (Figure 1).

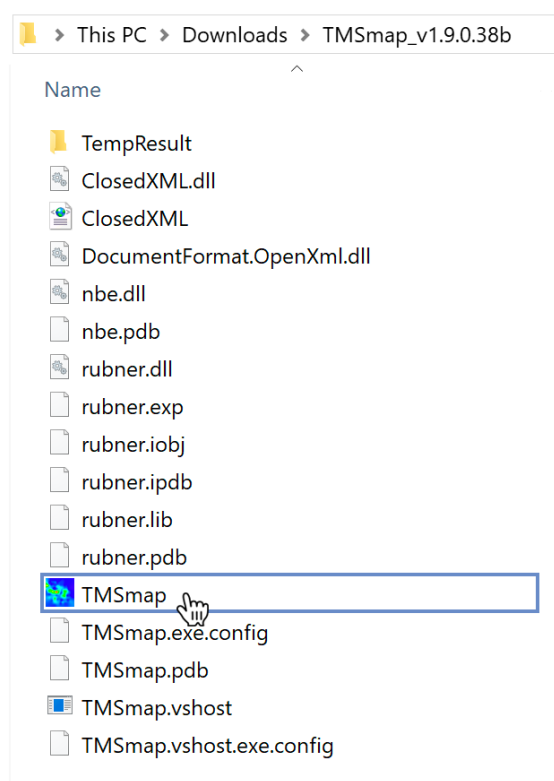


Figure 1 Application start

After successful run one can see the main window of the application. There are 2 tabs in the main window: **Data** (data loading and preprocessing) and **Maps** (maps creation, estimation and comparison) (Figure 2). In the main menu on the top of the main window you can see 4 buttons: **File**, **Settings**, **View** and **Info**.

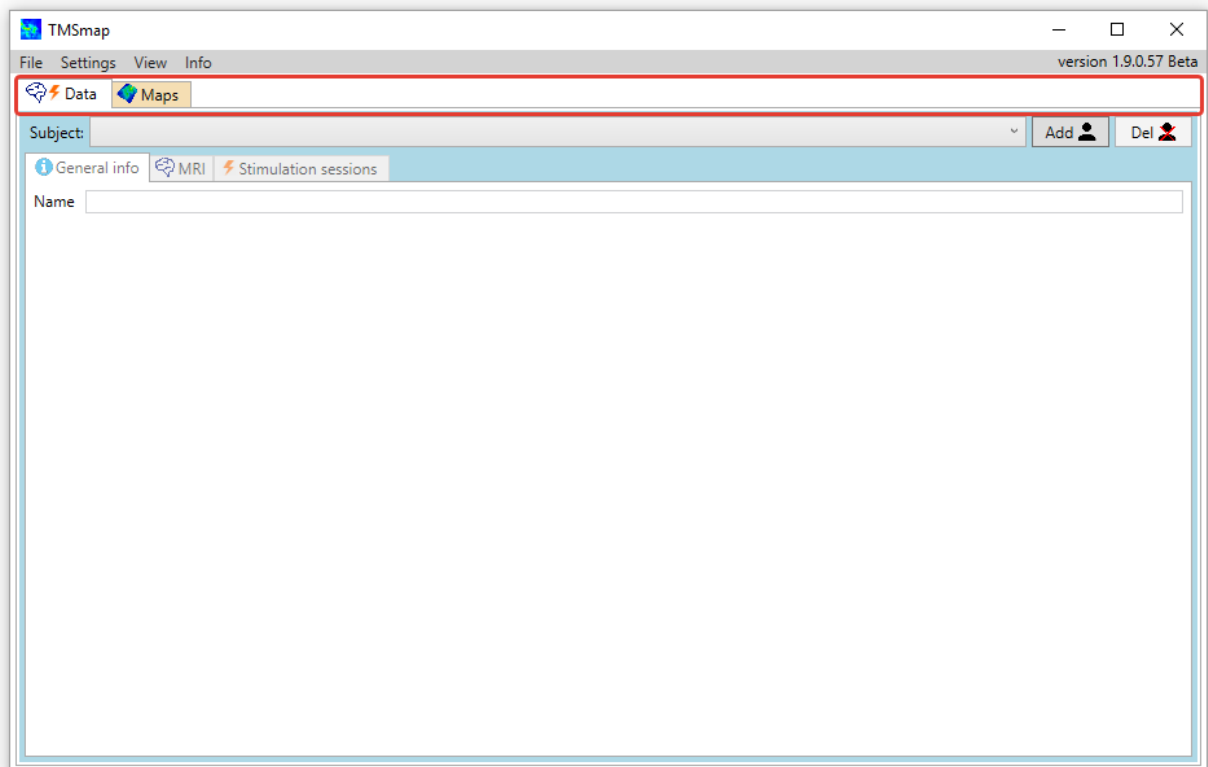


Figure 2. Main window: Data and Maps tabs

## 8 Main menu

### 8.1 File

One can use **Quit** button in the **File** submenu to close the application, alternatively, one can press **Alt+F4** keys combination (Figure 3).

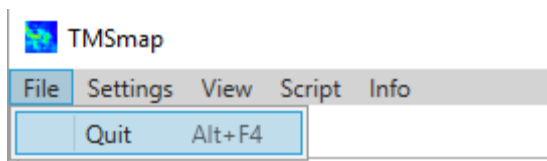


Figure 3. Main menu: File

### 8.2 Settings

Using **Settings** button in the main menu (Figure 4), one can change the following settings:

- the directories for stimulation data, MRI and temporary results storage (Figure 5);
- background color (Figure 6);
- neuronavigation system type (Figure 7);
- parameters (Figure 8);
- type of the color gradient for maps output (5 or 7 colors rainbow, bipolar from Yellow to Blue, etc.) (Figure 10).

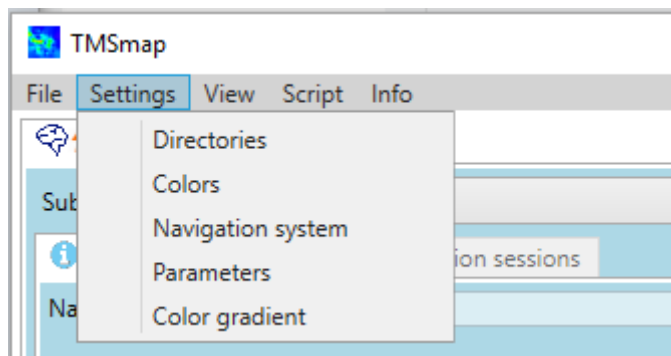


Figure 4. Main menu: Settings

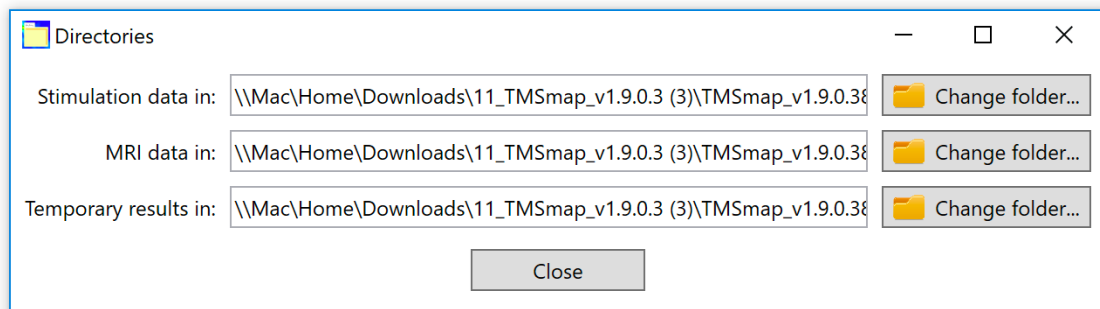


Figure 5. Directories settings

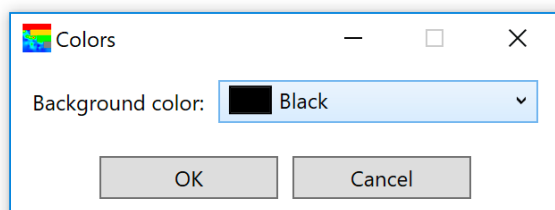


Figure 6. Background color settings

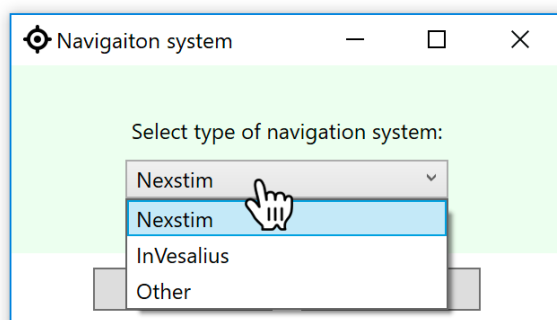


Figure 7. Navigation system type selection

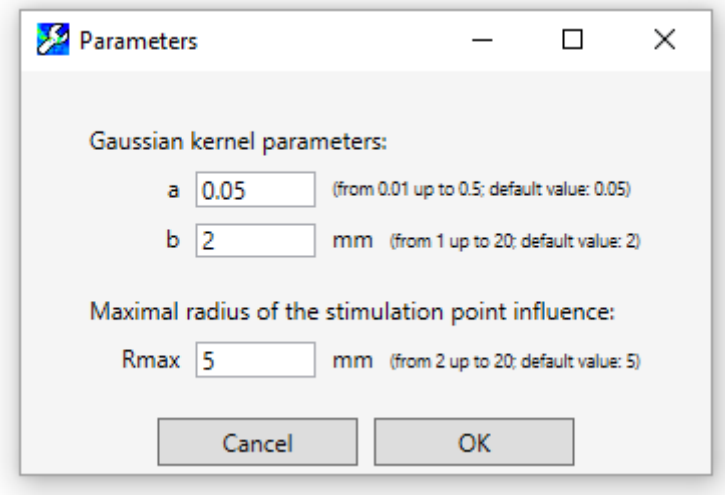


Figure 8. Parameters settings

Navigation system type is required for correct coordinates loading. For example, one can see the differences between MRI CS (RAS) and InVesalius Navigator CS (Figure 9).

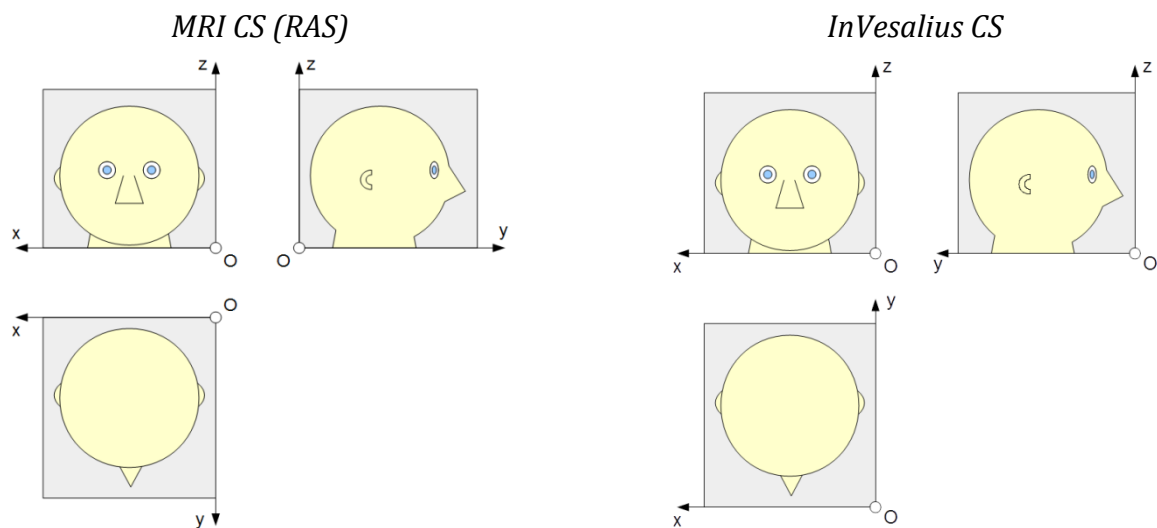


Figure 9 MRI and InVesalius Neuronavigator coordinate systems

TMSmap software at the moment supports three neuronavigation systems: Nexstim, Localite Navigator and InVesalius Navigator. For all other neuronavigation systems data (select **Other** item, Figure 7) it is possible to recalculate the coordinates provided by the navigation system to those used in TMSmap (origin - left posterior inferior corner; axis - Left to Right (x axis), Posterior to Anterior (y axis), Inferior to Superior (z axis) to be able to coregister MRI and coil positions.

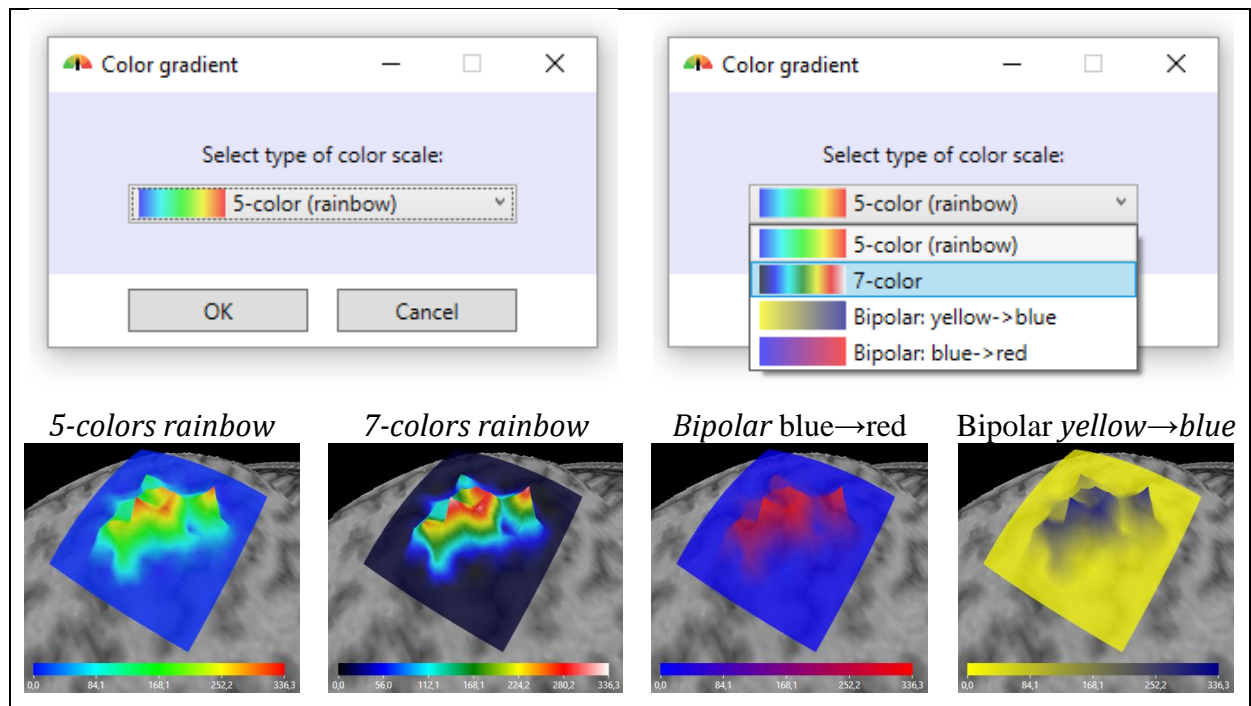


Figure 10 Color gradient types

Also TMSmap software at the moment supports four types of color gradient for map creation: 5 and 7 colors rainbow, bipolar from yellow to blue and bipolar from blue to red (Figure 10).

### 8.3 View

One can use **Full screen mode** button in the **View** submenu to close the application or press **F11** key (Figure 11).

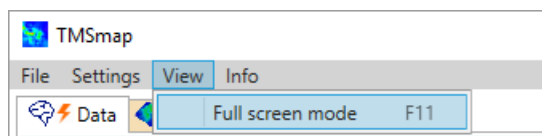


Figure 11. Main menu: View

### 8.4 Info

**Info** submenu contains **Help**, **License** and **About** buttons (Figure 12).

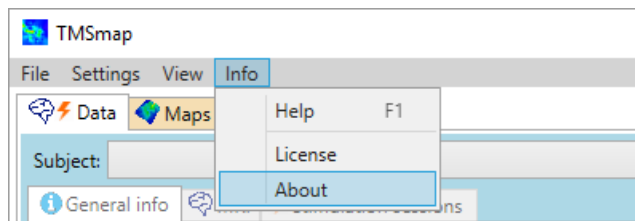


Figure 12. Main menu: Info



## 9 Load data

### 9.1 Preparation

To create a representation map you need Stimulation data in .nbe or .xlsx formats and, optionally, MRI data in .nifti format (.hdr and .img files) for map visualization above the cortical surface.

A stimulation data should contain the coordinates of the stimulation points which, in the simplest case, can be just coil's coordinates on the scalp, as well as the coordinates of the estimated electric field (EF) maximum in the brain.

Current version of TMSmap is primarily designed for motor mapping data. In this case the channels should contain the information about the MEP characteristics such as peak-to-peak amplitude, latency, duration, number of peaks etc. However, any type of the categorical parameters such as "Yes" (=2), "No" (=1) e.g., when inducing phosphenes or error types - can also be used as a response value .

Exemplary data are in the .zip folder **Example\_Data\_for\_TMSmap\_v....** Extract them before using.

### 9.2 New subject

Choose **Data** tab. To create a new subject, click on **Add** button (Figure 13). Go to **General info** subtab and customize the general information (ID and Name) about the subject if it's needed.

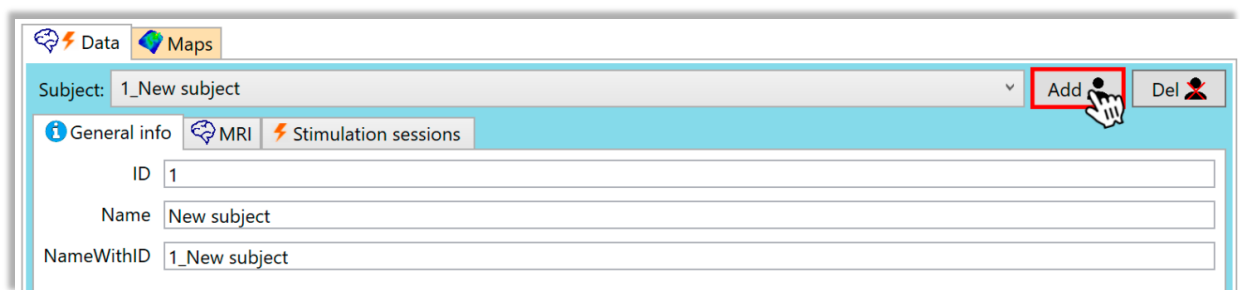


Figure 13. Creation of a new subject

### 9.3 MRI data

MRI is optional. TMSmap supports NIFTI (.nii or .hdr/.img file format).

Choose **Data** tab. Go to MRI subtab. Upload MRI data for the subject by clicking the **Browse** button (Figure 14).

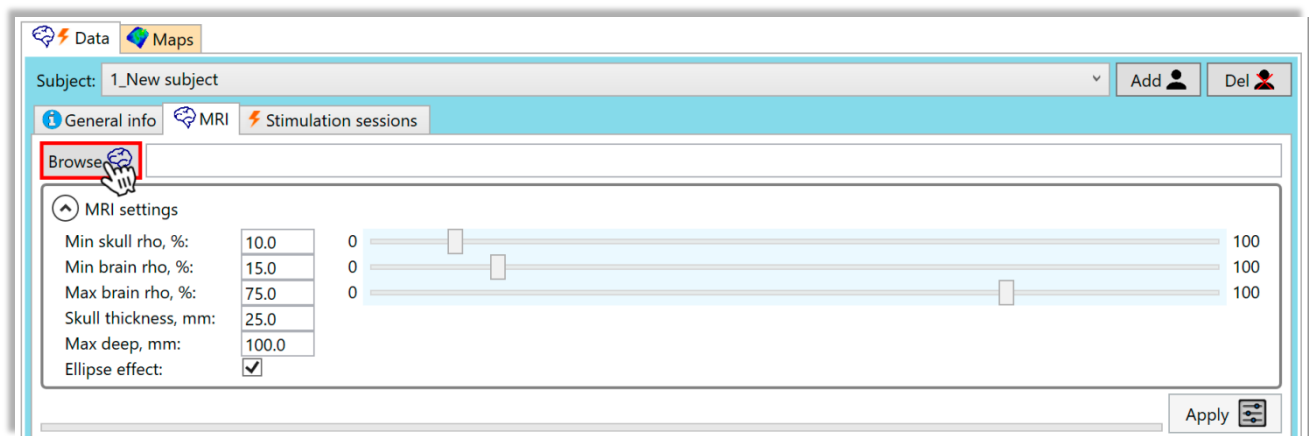


Figure 14. MRI data uploading (Rho ( $\rho$ ) represents density)

To upload the exemplary data, please choose file *Pavel.hdr* in the folder **MRI\_data** in the path: **Example\_Data\_for\_TMSmap\_v...** > **MRI\_data** (Figure 15).

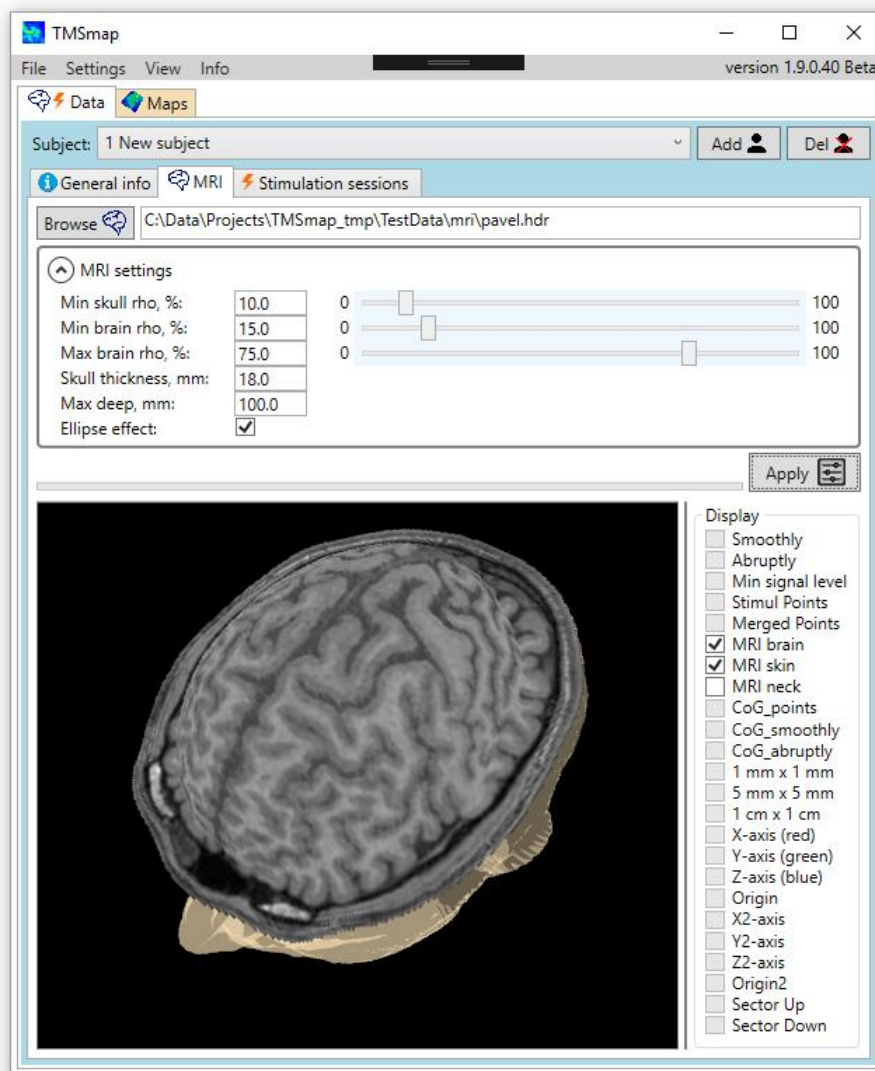


Figure 15. Example of uploaded MRI

MRI parameters are automatically found. In case the visualization is not optimal, it is possible to change them. Peeling is usually defined from 20 to 30 mm depending on the depth which was chosen during the stimulation procedure, so all the stimulation points are visualized above the cortical surface.

On the panel **MRI settings** one can change such indicators as **Skull rho**, **Min brain rho**, **Max brain rho**, **Skull thickness**, **Max deep**. To apply this setting click icon **Apply** at the lower right corner of the panel (Figure 14).

## 9.4 Stimulation sessions data

Go to the subtab **Stimulation sessions** and click **Add** button (Figure 16).

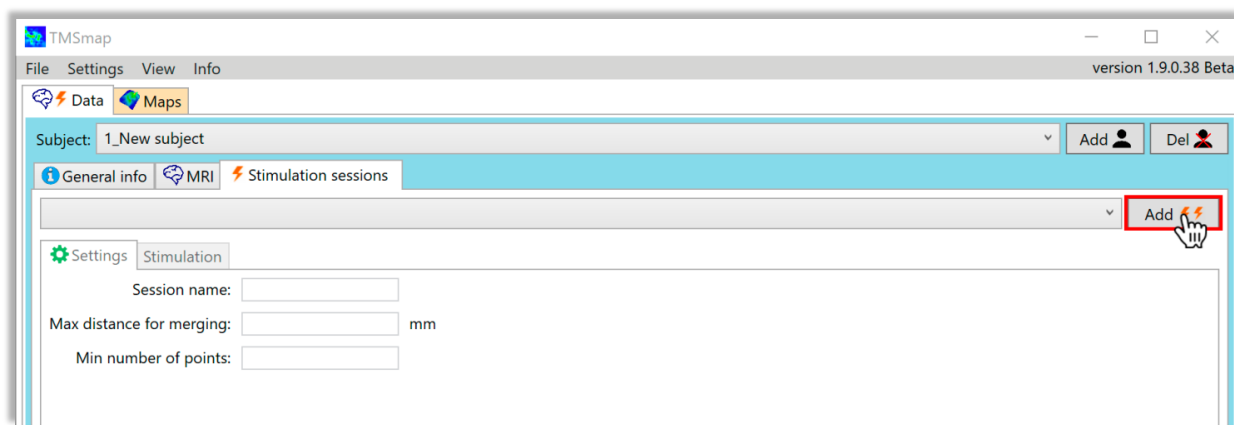


Figure 16. Creation of a stimulation session

Here you can change sessions' names and set up the parameters: **Max distance for merging** ( $R_{\text{merge}}$ , mm) and **Min number of points** ( $N_{\text{merge}}$ ) (Figure 17).

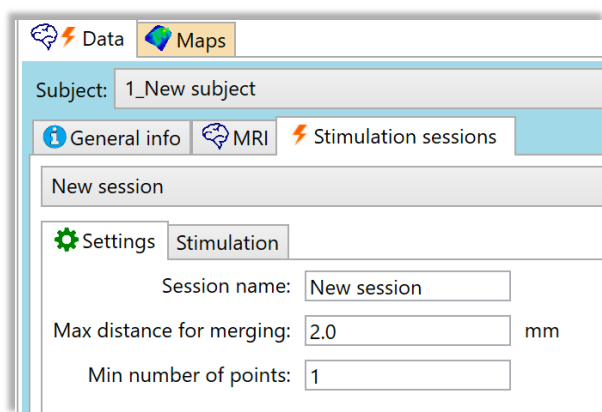


Figure 17. Settings for stimulation sessions

Example of the merging of the nearest points is shown on Figure 18.

$R_{\text{merge}}$  distance default value is 2 mm which is based on the best possible accuracy of the navigation system. The user can set this parameter being equal to any non-negative value. In case of the  $R_{\text{merge}}$  being equal to zero, points will not be merged. After the merging procedure TMSmap will take into account only such merged points which have at least

$N_{\text{merge}}$  repetitions of the stimuli. In case there is no need to take into account points with several stimulation repetitions, it is possible to set this parameter equal to 1.

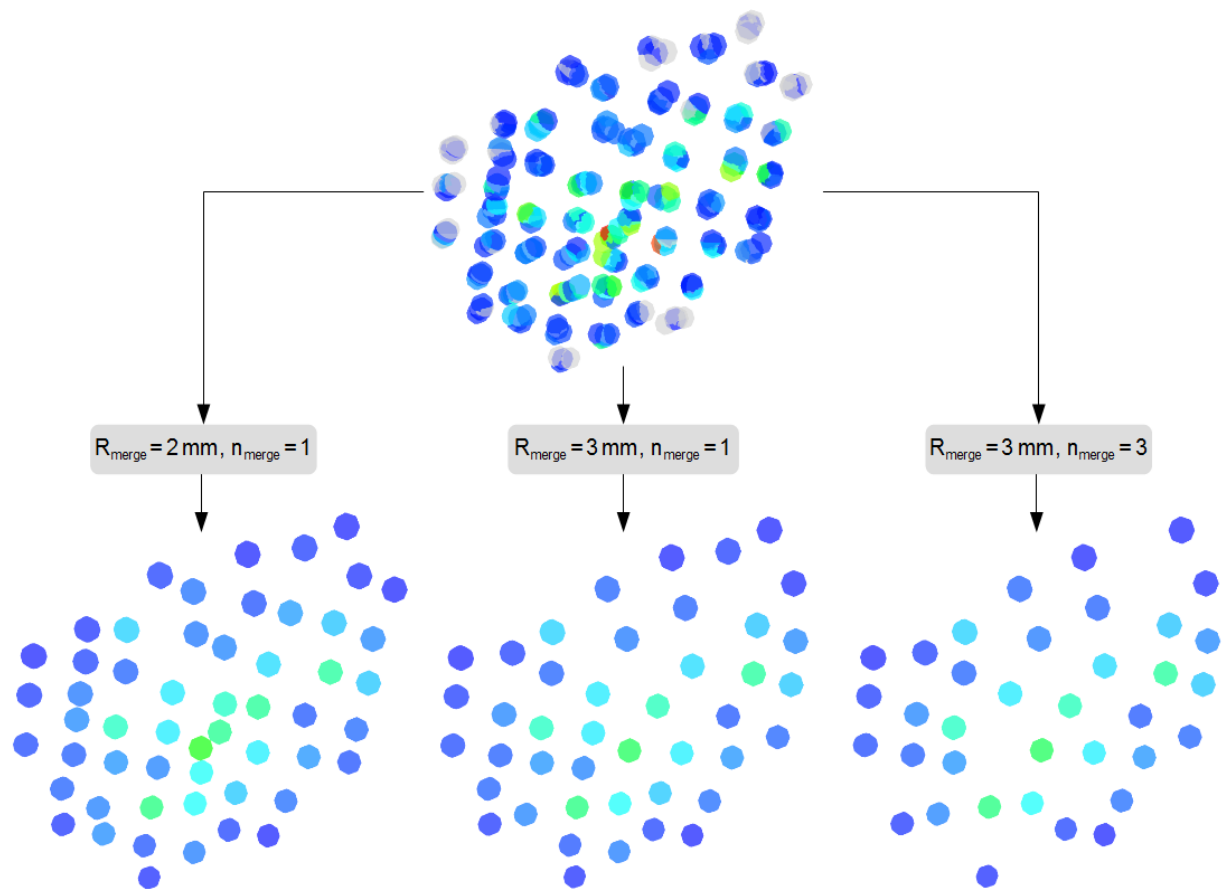


Figure 18. Merging of the stimulation points with different parameters ( $R_{\text{merge}}$  – max distance for merging,  $n_{\text{merge}}$  – min number of merged points to taking into account for map construction)

In the section **Stimulation** you can upload stimulation sessions data. Press the **Add** button and choose .nbe, .csv or .xlsx files that you need (Figure 19).

The exemplary data one can find in the path: **Example\_Data\_for\_TMSmap\_v...->Stimulation\_data->nbe** or **Example\_Data\_for\_TMSmap\_v...->Stimulation\_data->xlsx** or **Example\_Data\_for\_TMSmap\_v...->Stimulation\_data->csv**.

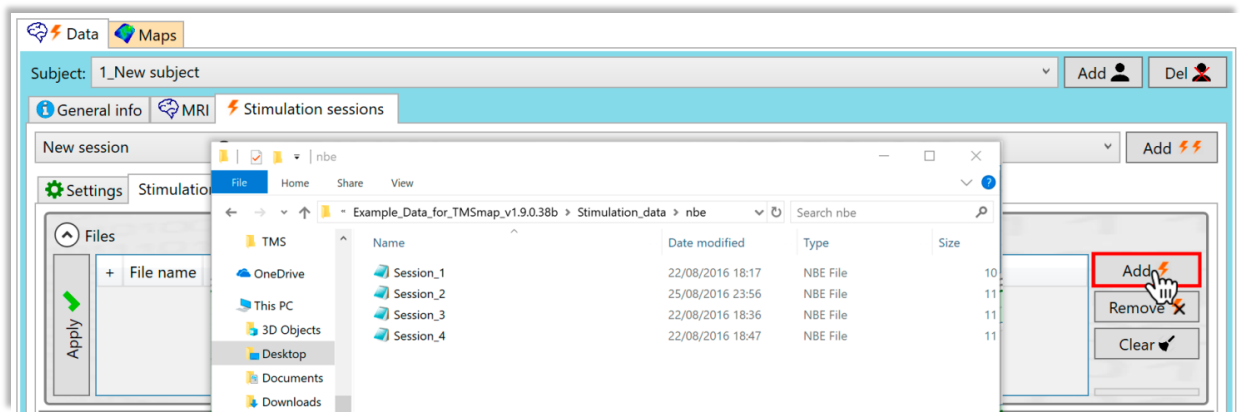


Figure 19. Stimulation sessions data uploading

Please select files which you want to use and click Apply (Figure 20).

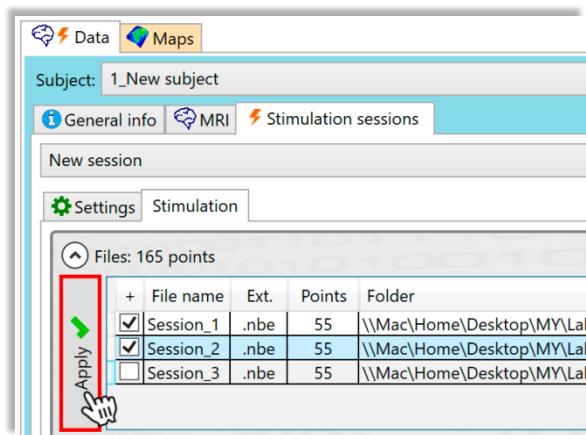


Figure 20. Stimulation sessions data application

On the panel “**Channel selection**” one can choose the desired channel for map construction. After channel selection one can see the points colour-coded depending on the response values (Figure 21).

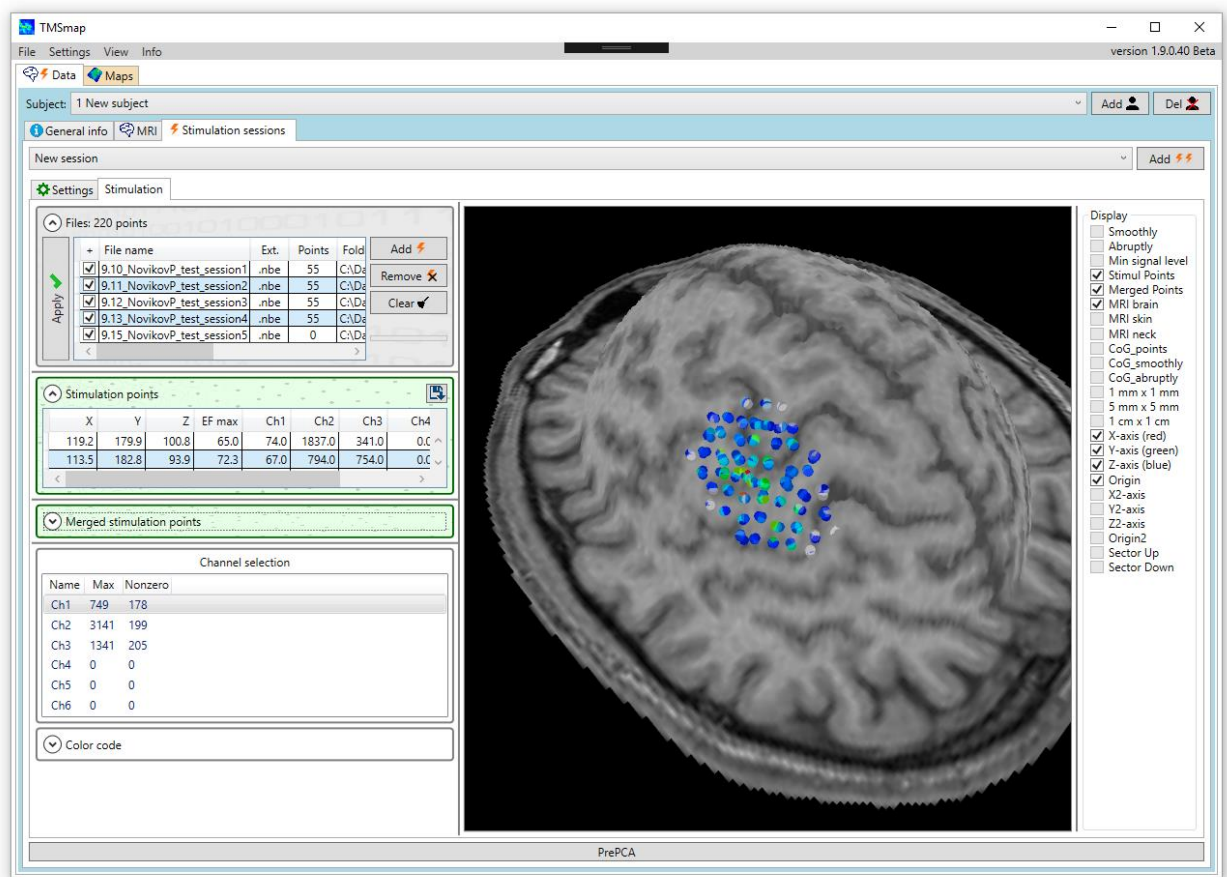


Figure 21. Channel selection

## 9.5 Load MRI and stimulation data automatically by script

Example of the script one can see in (Figure 22).

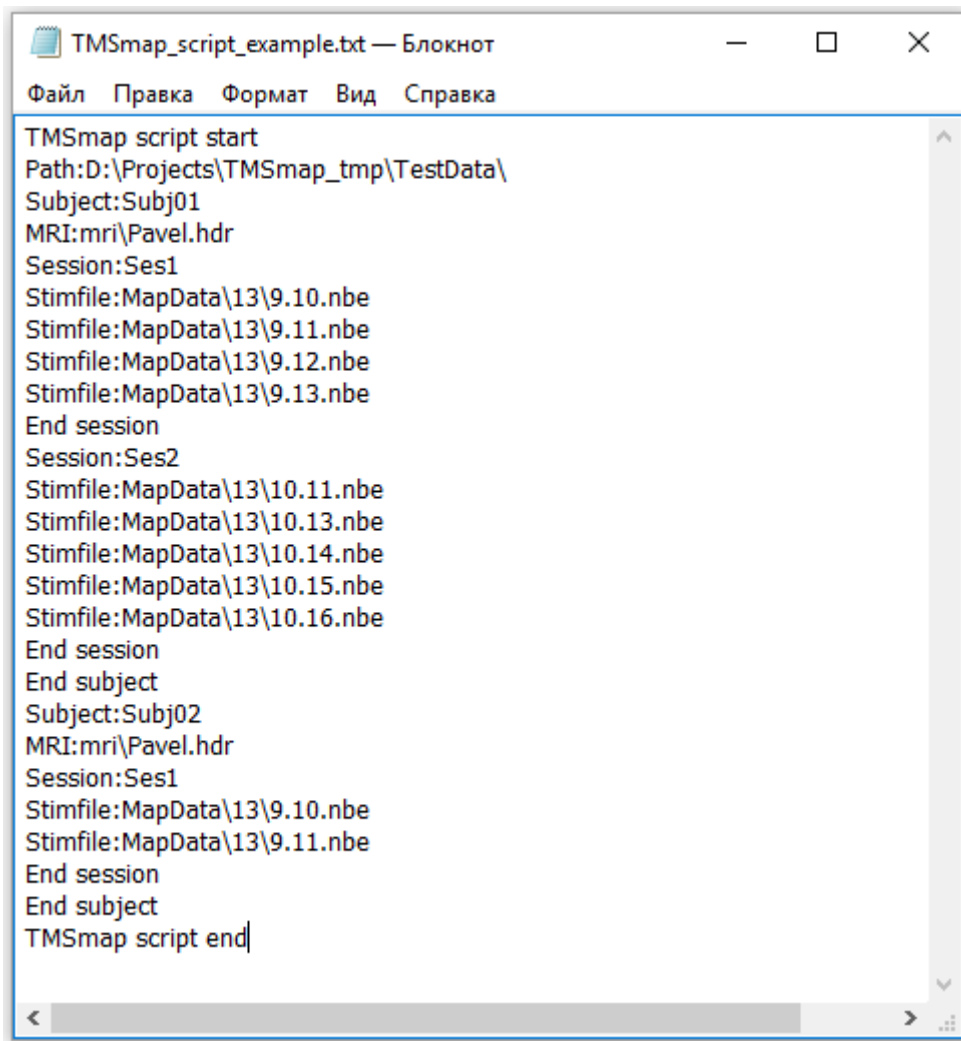


Figure 22. Example of the script for automatic data downloading

Go to the **Script** in Main menu (Figure 23) and click **Run script (MRI, Stimulation files)...** . Automatic data loading to the software should start. After downloading, click **Run script (Apply)...** .

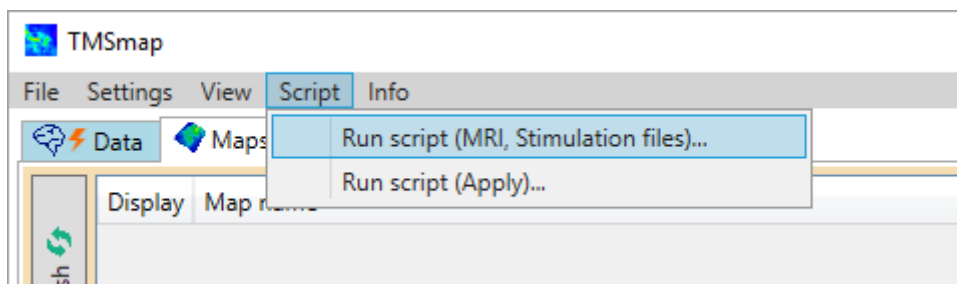


Figure 23. Script menu

## 10 TMS maps construction

To construct a map, please press the **Add** button and choose subject, session and channel that you need (Figure 24). One can add more than one map and browse them

simultaneously.

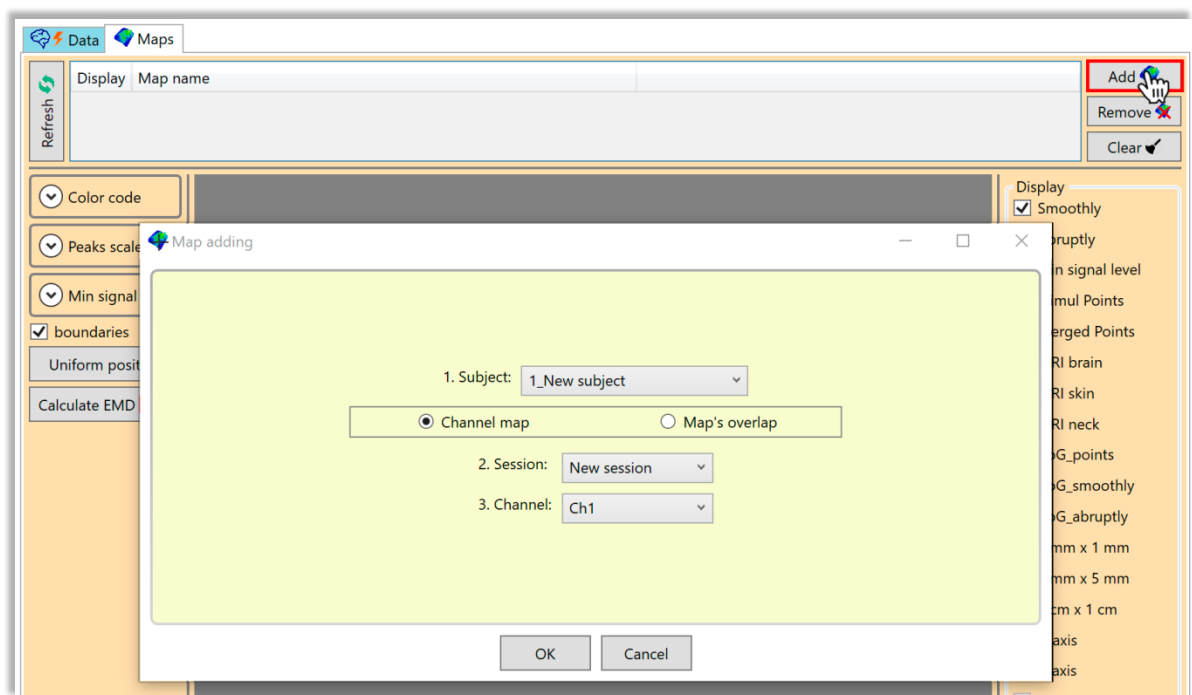


Figure 24. Map adding

To browse a map, tick ones from added that you need and click the **Refresh** button (Figure 25).

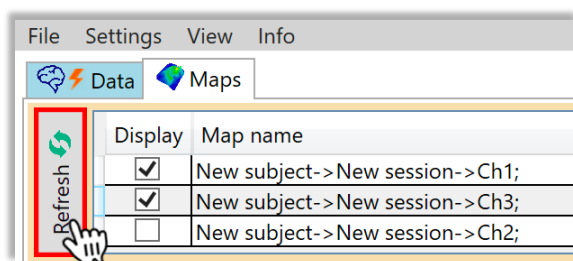


Figure 25. Refresh maps output

For the results view (response areas, volumes, overlaps, points, map shape, CoGs, etc.) choose the corresponding checkboxes. Also one can set up colour-code, peaks scale and min signal level (Figure 26).



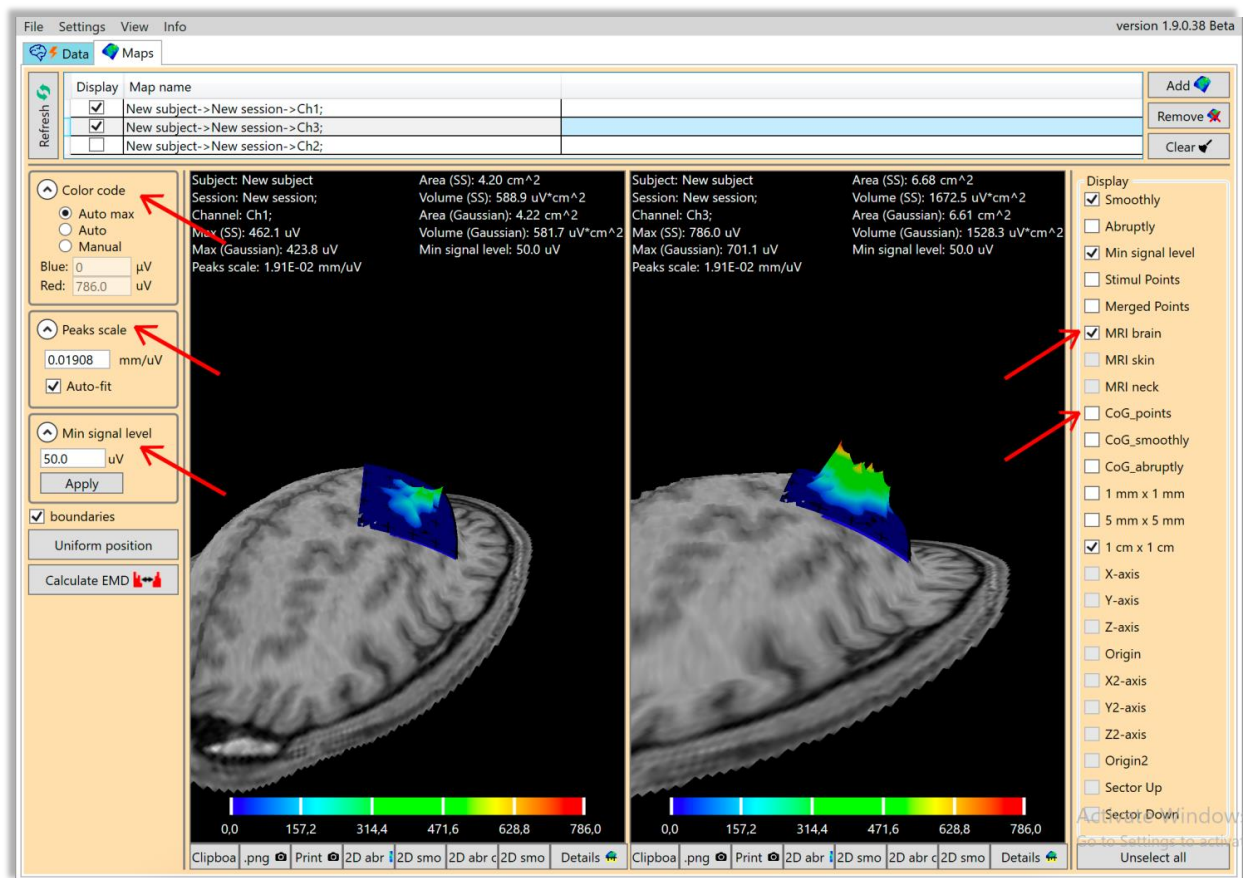


Figure 26. Results view

There are two approaches of the map generation in the TMSmap software:

1) based on the assumption of the smoothly changing response function among the points. In this case for the surface construction an approach allowing to create a maximally smooth surface going through all the points – approximation based on smoothing (ABOS) method is used (Dressler, M. M. (2009). Art of Surface Interpolation. Available at: <http://m.dressler.sweb.cz/AOSIM.pdf>). For visualization please select **Smoothly** button on the **Display** panel;

2) on the assumption that the response function may change abruptly from one point to another. In this case, the constructed surface would be built as a combination of the gaussian kernels surfaces defined by the exponential function created from each stimulation point (Figure 27); for visualization select **Abruptly** button in the **Display** panel.

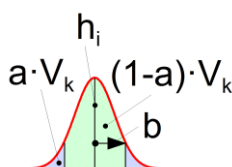


Figure 27. Gaussian kernel parameters (axial cross section view): a – the portion of the whole kernel volume  $V_k$  located outside the radius b,  $h_i$  – response value. Hereby, b is the navigation accuracy in (1-a) portion of all the cases. One can change values of these parameters (a and b) using Parameters window (Figure 8). The default TMSmap settings for a – 0.05 and for b – 2 mm. It means that only 5% of the whole kernel volume would be more than 2mm further from the stimulation point, indicating 95% probability for the real stimulation point to be at this given area. The default value of

the radius  $b$  is based on the best possible accuracy (an error acceptable for a concrete navigation system, e.g. 2 mm - for Nexstim system).

For any site which is further away from any stimulation point over the distance bigger than **Maximal radius** (Figure 8), the software will put an artificial stimulation point with the response equal to zero. The default value for this parameter is 5 mm which is a reported average error for frameless stereotaxic systems.

Please use **Min signal level** (Figure 26) textbox to set the threshold for the constructed map. In TMSmap default value (for MEP) of the threshold is 50  $\mu\text{V}$ .

## 11 Earth mover's distance (EMD) calculation

Map surface could be characterized by its individual 3D profile. TMSmap allows numerical comparison of the profiles of the constructed maps using the so-called Wasserstein metric or EMD. EMD is a minimum amount of work needed to shift one distribution to another. EMD may be useful to numerically differentiate maps located nearby to each other. These maps might be similar in terms of the standard parameters such as areas and volumes but still varying due to the complexity of their excitability profiles.

### 11.1 EMD metric normalization

Two maps are normalized by volume automatically before calculating EMD between them. Then EMD is calculated and represented as a relative value – a percentage of the EMD between two extreme maps each consisting of the only one peak maximally separated from each other in the limits of the individual size of the “active area”. For each subject individually TMSmap defines “active area” in a following manner: it includes any stimulated point where in at least one channel in at least one session was a response with the amplitude higher than a chosen threshold (e.g. MEP amplitude > 50  $\mu\text{V}$ ). A maximal distance between the points in such active area is taken as an individual constant for the EMD normalization.

### 11.2 EMD calculation

To calculate EMD between maps:

1. Choose **Maps** button and press **Add** button (Figure 24).
2. Choose subject and select **Map's overlap** option in the **Map adding** window.
3. Define which two maps should be constructed and compared using sessions and channels lists and press **OK**.
4. In the simple/overlap maps list on the top of the **Maps** tab select new overlap map and press **Refresh** button.
5. After several seconds one can see new overlap map in the centre of the **Maps** tab.
6. Press **Calculate EMD** button. After several seconds one can see EMD values on the top of the overlap map visualization.

7. As well one can press **Details** button to see the table with EMD values’.

## 12 Transfer stimulation data and maps to MNI brain model for cross-subjects analysis

Functionality is available in the software. Description is under development.....

## 13 Version history

### 13.1 From version 1.9.0.44b to version 1.9.0.70b

The following most significant changes have been added:

- mean, median or max criteria for merging stimulation points (before: mean criterion only);
- different color gradients for maps output;
- the ability to show subject’s face on the Stimulation tab;
- the ability to show axes and origin of the coordinate system of the selected navigation software type;
- button to delete a stimulation session from the list of stimulation sessions;
- the ability to output maps with different horizontal scale in the Maps tab;
- buttons to show all maps or one map in software window;
- output of the parameters of all selected maps in one table (**Maps details** button);
- support single file NIFTI (.nii format), before: .hdr/.img format only.

### 13.2 From version 1.9.0.70b to version 1.9.1.0b

The following most significant changes have been added:

- support .csv file format for stimulation data;
- transfer stimulation data to MNI brain model for cross-subjects analysis (SPM8 is needed for individualized MNI brain models creation);
- the ability to load MRI and stimulation data for several subjects automatically by script;
- support forming and sending emails with map pictures from GUI (**Send** button).

## 14 Acknowledgements

Authors are deeply grateful to Dr. Alexey Ossadchii and Dr. Andrey Zhdanov for discussions. Authors are also grateful to Dr. Victor Hugo Souza and Renan Matsuda, MS for the data from the navigation system “InVesalius” provided for testing. We acknowledge Dr. Yossi Rubner for the open-source code for EMD calculation the modification of which we used. Authors are also grateful to students Daria Pozdeeva, Ekaterina Ivanina and

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## 15 Contacts

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Maria Nazarova, MD, PhD (e-mail: [chantante@gmail.com](mailto:chantante@gmail.com)) – supervisor  
Vadim Nikulin, PhD – scientific consultant

or use a special form (<http://tmsmap.ru/index/0-3>) at the website.

