

EVALUATION OF RESPONSE AREAS OF AUDITORY NEURONS

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Abstract

In the auditory pathway, the response properties of neurons are commonly assessed using tonal stimuli with varying frequency and intensity. In such a case, the responses to tones may be plotted in a form of a two-dimensional function of frequency and intensity, the so called frequency-intensity response area (FIRA). We present a MATLAB tool for evaluation of neuronal FIRAs. The tool features a novel approach to FIRA evaluation that allows to significantly reduce the temporal costs of the experiment while retaining the desired accuracy of assessment of the response parameters, making the measurements safer and more efficient. The tool employs a MATLAB graphical user interface.

1 Measurement of neuronal response properties

The responses of auditory neurons to sounds may be rather complex and in general, they are not time-invariant. Even for a stationary tonal stimulus, an adaptation of response magnitude is observed at several time scales [1]. Furthermore, the response properties are dependent on the history of previous stimulation in several ways; first, a preceding stimulus may suppress or facilitate the neuron's response to the current stimulus; second, the neurons are able to adapt to the stimulus statistics, tuning their sensitivity to the most prevailing sound [2]. It follows from the previous facts that the parameters of the stimulation that affect the neuron's response are numerous. To get an insight to the function of the entire system, however, it is necessary to keep the number of parameters at a reasonable level. For this reason, certain simplifications have to be accepted when evaluating the neuronal response properties.

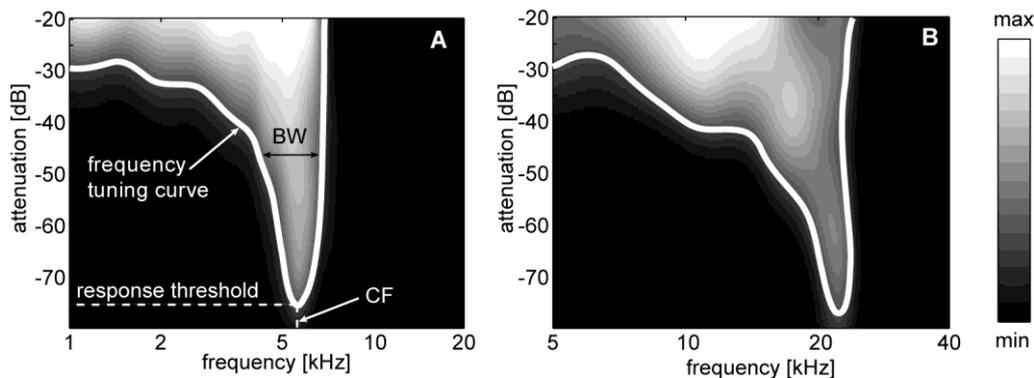


Figure 1: Two typical examples of neuronal frequency-intensity functions. The response magnitude is marked with the shades of grey, white and black corresponding to a maximum and a minimum response, respectively. Solid white lines mark the so called frequency tuning curve. Response threshold, characteristic frequency (CF) and bandwidth of the passband (BW) are shown.

The response properties of auditory neurons are often assessed using short tonal stimuli with variable frequency and intensity. This approach usually assumes that neuronal responses are time-invariant; in such a case, the responses to tones may be plotted in a form of a two-dimensional function of frequency and intensity, obtaining a description of the neuron that is similar to a filter transfer function. The resulting function is called frequency-intensity response area (FIRA). A FIRA provides the basic characterization of a neuron that may be easily interpreted. It also serves as a basis for extraction of various response parameters, such as the bandwidth of the passband (denoted as BW in Fig. 1), frequency tuning curve, response threshold, characteristic frequency (denoted as CF in

Fig. 1), response-intensity functions, etc. Two examples of neuronal response areas are shown in Fig. 1 [3]. Apparently, the neurons respond only to certain combinations of frequency and intensity; furthermore, the response magnitude is not uniform inside the response area. On the other hand, for certain frequency-intensity combinations, the neuron's activity may be suppressed (inhibited). The remaining frequency-intensity combinations leave the neuron's activity unaffected and the neuron exhibits only its spontaneous activity.

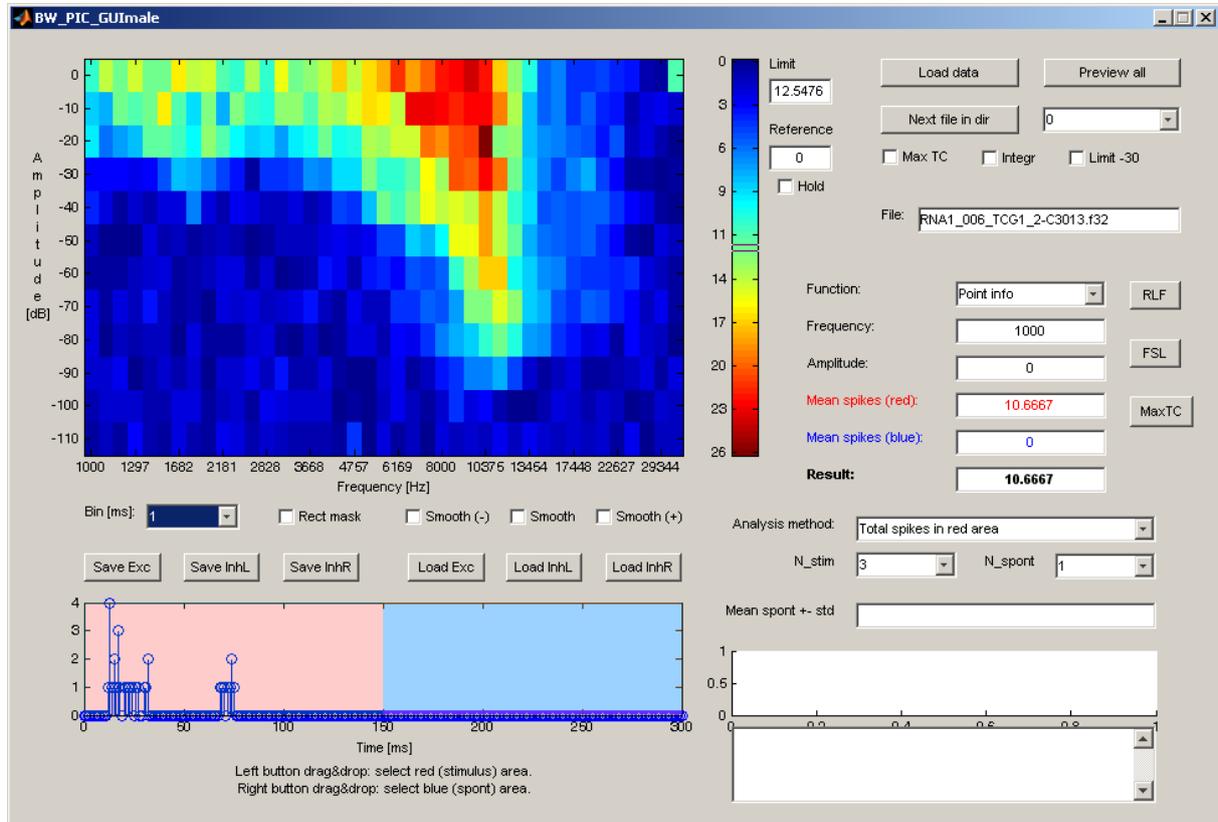


Figure 2: Main window of the graphical user interface. An unsmoothed (raw) FIRA is shown in the top-left corner. A FIRA is a 2-D function of frequency and intensity that is initially defined only on a limited number of points. The FIRA is computed from the first 150 ms of the recorded response. PSTH bin width is set to 1 ms.

To obtain a frequency-intensity response area, a neuron has to be stimulated several times for each combination of frequency and intensity. The combinations of frequency and intensity vary randomly to cover the desired area of frequencies and intensities. Considering that to obtain a FIRA covering with a reasonable resolution the entire responsive range of a neuron, several hundred points have to be measured. This process may be time-consuming, furthermore, due to the animal's movements, the responses of neurons may not be stable. For these reasons, a need to shorten the measurement time arises.

Last but not least, it is often necessary to evaluate huge amounts of neuronal data. To reduce the time needed for evaluation as much as possible, advanced software tools have to be employed. The presented MATLAB tool represents a custom software solution that fulfills all the requirements given by routine neurophysiological practice of the Department of Auditory Neuroscience at the Institute of Experimental Medicine of AS CR.

2 Assessment of the frequency-intensity response area

As was pointed out above, the neuronal responses to stationary stimuli are not time-invariant. A typical response consists of a strong response onset followed by a decrease to a steady-state activity; the response types are nevertheless numerous. The temporal pattern of the response is usually described in the form of a peristimulus time histogram (PSTH), which plots the neuron's activity over time averaged in short time bins. The presented tool can show the PSTH of any measured FIRA point (see Fig. 2), it is possible to set the PSTH bin width from 0.01 to 10 milliseconds. In Figs. 2 and 3,

different settings of PSTH bin width are shown. The depicted neuron has a strong onset response followed by a pause in activity and a pronounced reaction at stimulus offset. It is apparent that the wider bin may hide the fine structure of the PSTH due to augmented averaging.

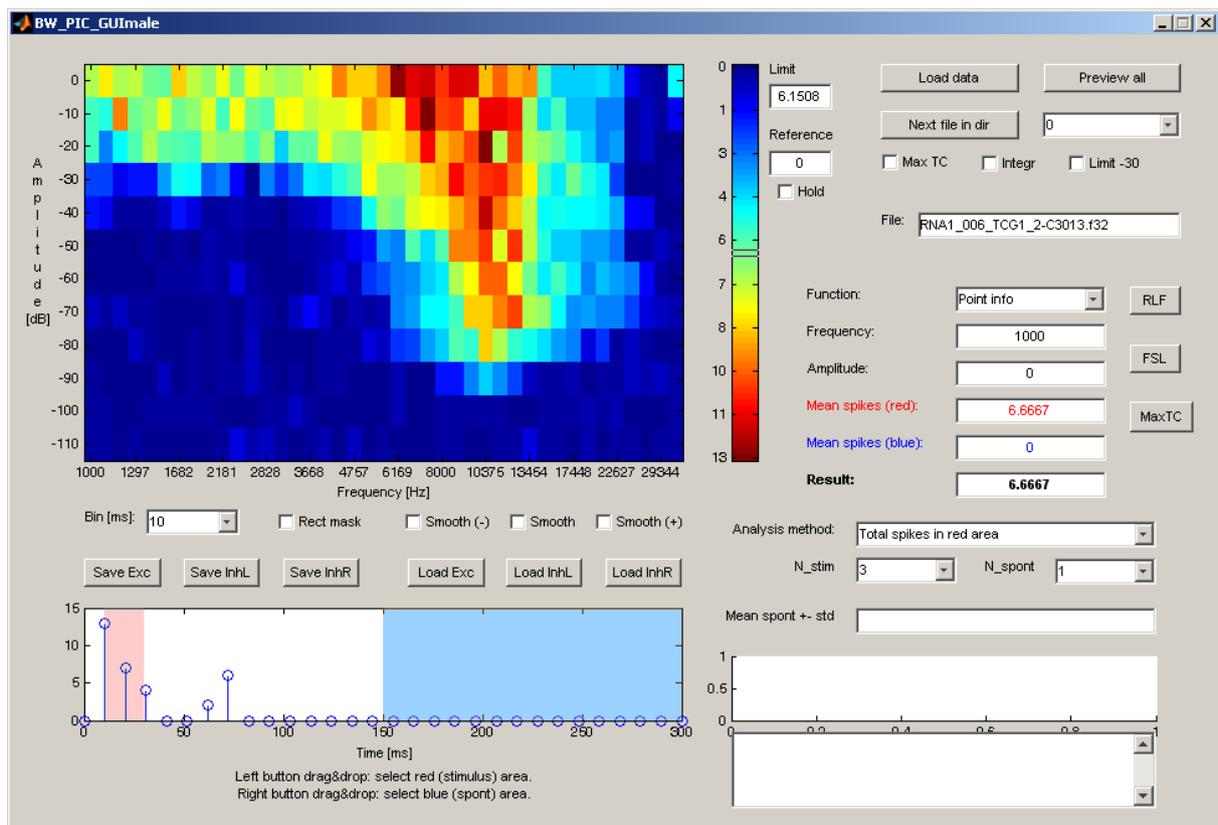


Figure 3: Main window of the graphical user interface. In this case, the FIRA is computed from the onset of the PSTH only, see also Fig. 2. PSTH bin width is set to 10 ms.

The FIRA may be computed from any portion of the recorded PSTH to exclude, for example, spontaneous activity before the signal onset, or to confine oneself to the steady-state response only, and so on. Typically, the whole evoked response to the stimulus is taken for the FIRA evaluation. The difference between two FIRAs of the same neuron that stems from different selection of PSTH portion are illustrated in Figs. 2 and 3.

In the PSTH window, it is possible to select two intervals:

- excitatory (red): this is used to select that portion of the PSTH where the evoked response to the stimulus is expected,
- spontaneous (blue): this is used to select that portion of the PSTH where the spontaneous activity is expected.

Two ways of FIRA computation are available:

- each point corresponds to averaged responses of the neuron computed from the excitatory (red) area of the PSTH,
- each point corresponds to averaged responses of the neuron computed from the excitatory (red) area of the PSTH minus averaged responses of the neuron computed from the spontaneous (blue) area of the PSTH.

The second evaluation method allows to identify the inhibitory regions of the FIRA, i.e., those frequency-intensity combinations for which the neuron's response is suppressed by the stimulus.

A FIRA is a two-dimensional function of frequency and intensity that is initially defined only on a limited number of points (see Figs. 2 and 3). Each point is assigned a value that corresponds to the averaged responses of the neuron to the respective combination of frequency and intensity. Due to limited time available during *in vivo* experiments, the number of points of the measured FIRA is

limited. The intensity resolution is usually not higher than 5 dB, the frequency resolution is commonly set to $\frac{1}{4}$ octave. Considering that, for example, the smallest noticeable sound intensity difference in cats or rats is approximately 1 dB [4, 5], intensity resolution of 5 dB is insufficient. To overcome this constraint, the presented tool employs two-dimensional smoothing of the raw FIRA (see Fig. 4). The smoothing is implemented using a 2-D smoothing spline interpolation applied on the FIRA matrix. This function allows to keep the number of measured points at a reasonable level, while attaining the desired frequency and intensity resolution by combining the information of adjacent points of the matrix. Three levels of smoothing are available in the tool.

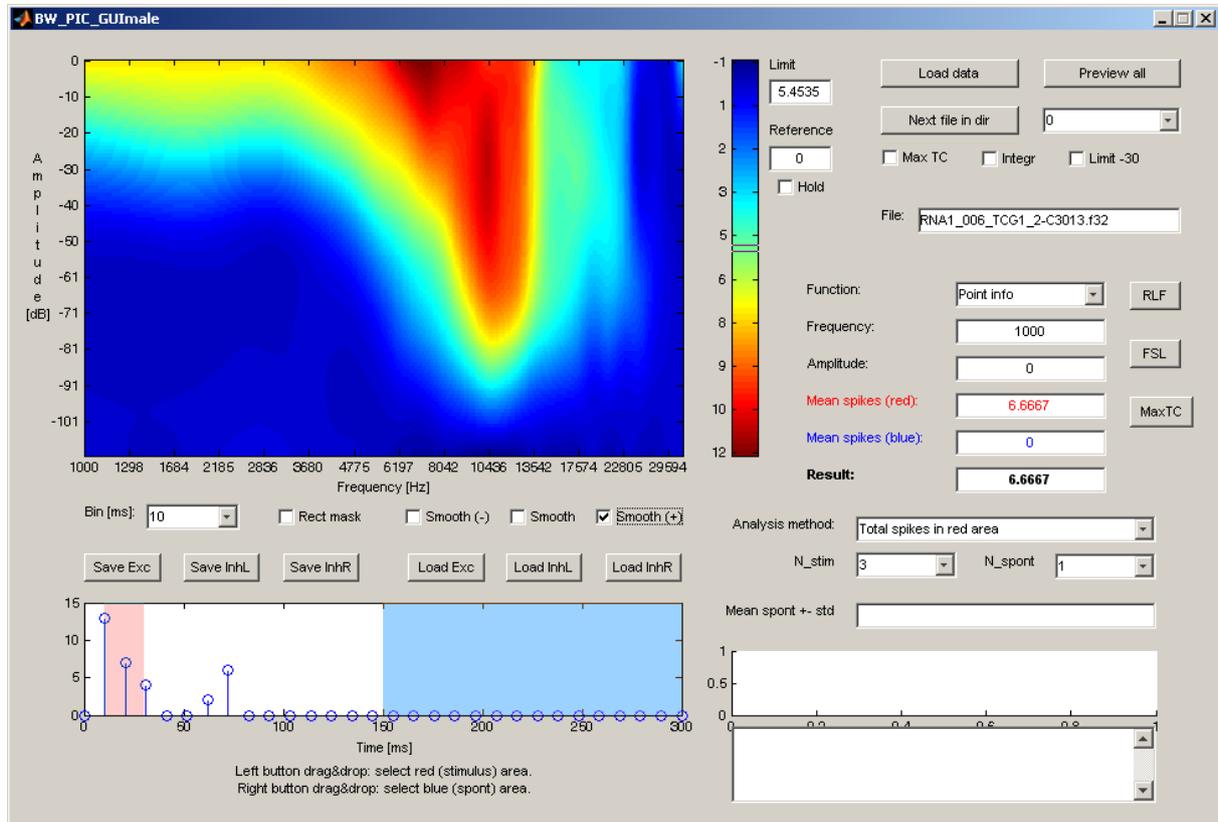


Figure 4: Main window of the graphical user interface. The settings of the FIRA evaluation are set analogously as in Fig. 3. A smoothed version of the FIRA is shown.

3 Extraction of response parameters

From a measured FIRA, either smoothed or raw, many response parameters may be extracted. The most common parameters include:

- response threshold: the minimum sound intensity for which the neuron responds;
- characteristic frequency (CF): the frequency at the response threshold;
- bandwidth of the tuning curve (BW): bandwidth of the neuron's passband assessed usually 10, 20, or 30 dB above the response threshold;
- maximum response magnitude, assessed usually either at CF or for the whole FIRA;
- first-spike latency: the delay between the stimulus onset and the onset of the evoked response, assessed usually for the point of the FIRA at the response threshold;
- spontaneous activity: the activity of the neuron during intervals with no stimulation;
- rate-intensity functions (response-intensity functions, RIF): dependence of the response magnitude on sound intensity, evaluated usually at CF

From a RIF, several additional parameters may be extracted:

- RIF type: strictly monotonic, saturating, or non-monotonic;

- i) RIF dynamic range: the increasing portion of the RIF between the response threshold and the point of saturation (see also Fig. 5);
- j) initial slope of the RIF, evaluated usually from the first 20 dB above threshold.

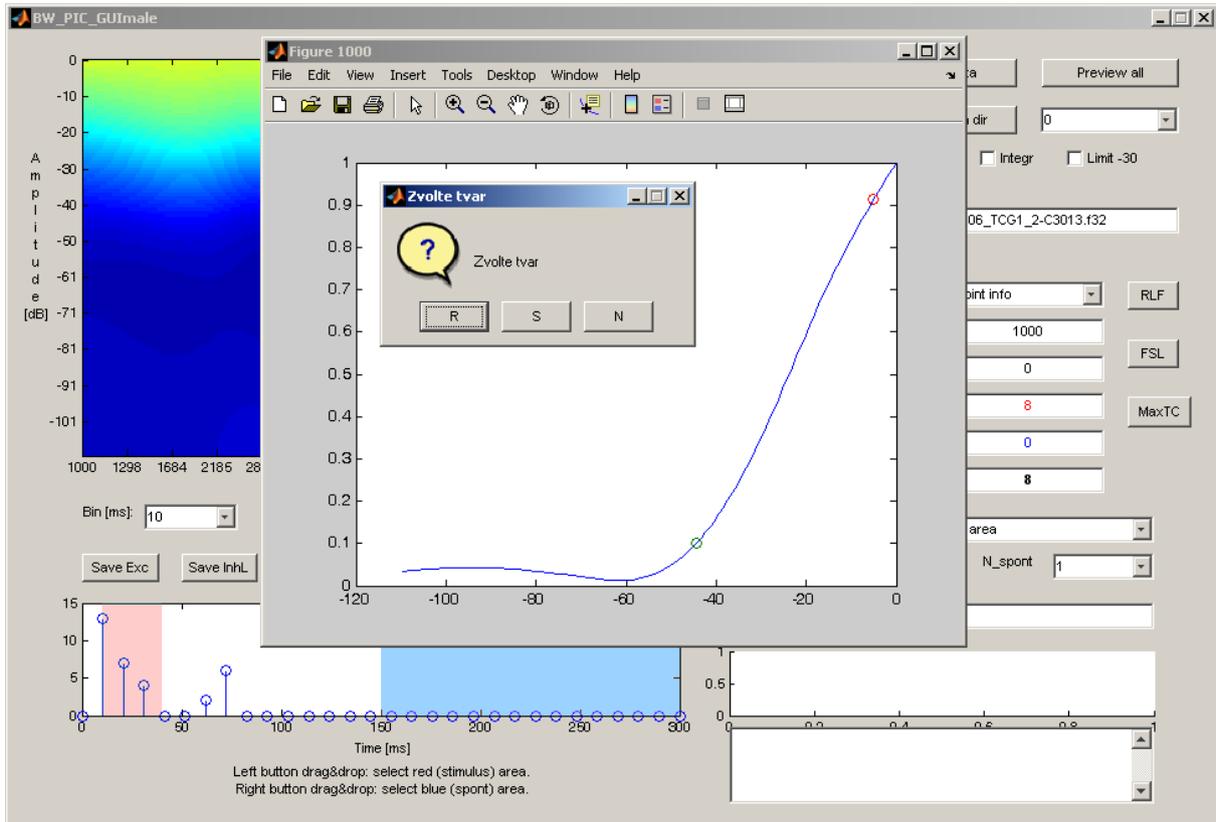


Figure 5: Evaluation of the RIF. The rate-intensity function was extracted from the smoothed FIRA at the characteristic frequency of the neuron. The dynamic range of the RIF is delimited with the green and red circles. An additional dialog window is shown in which the user can choose whether the RIF type is strictly monotonic (R), saturating (S), or nonmonotonic (N).

One of the most beneficial features of the presented tool is the FIRA spline smoothing, which represents a novel approach to FIRA evaluation. Therefore, most of the above mentioned parameters are extracted from the smoothed version of the FIRA.

Parameters given at points a), b), and c) have to be extracted from the so called frequency tuning curve – an outline of the FIRA (see Fig. 1). In order to provide an automated evaluation of the tuning curve from the underlying FIRA, an algorithm was implemented which detects the enclosed continuous area of the FIRA lying above a selected threshold – a suprathreshold area. The detected area is filled with a unique color red and all the necessary parameters are automatically extracted (see Fig. 6). Two ways of suprathreshold area detection are available:

- manual: a threshold is set manually (see section Graphical user interface), subsequently, the area is filled after clicking *inside* the expected suprathreshold area in the FIRA – this allows to overcome the problem of several disjoint suprathreshold regions within one FIRA,
- automated: a threshold is computed from the statistics of the neuron's spontaneous activity, subsequently, all regions of the FIRA lying above the threshold are filled

4 Graphical user interface

The tool is provided with a graphical user interface to increase the efficacy and to make the evaluation more convenient. The largest part of the window is devoted to the FIRA and the color scale which shows the range of response magnitudes in the given FIRA. Below, the control of the smoothing and PSTH bin width is shown, as well as the PSTH window. In the PSTH window, any portion of the recorded activity may be selected to mark the evoked response (red box), additionally, it

is possible to select the portion of PSTH corresponding to the spontaneous activity (blue box), see also section Assessment of the frequency-intensity response area.

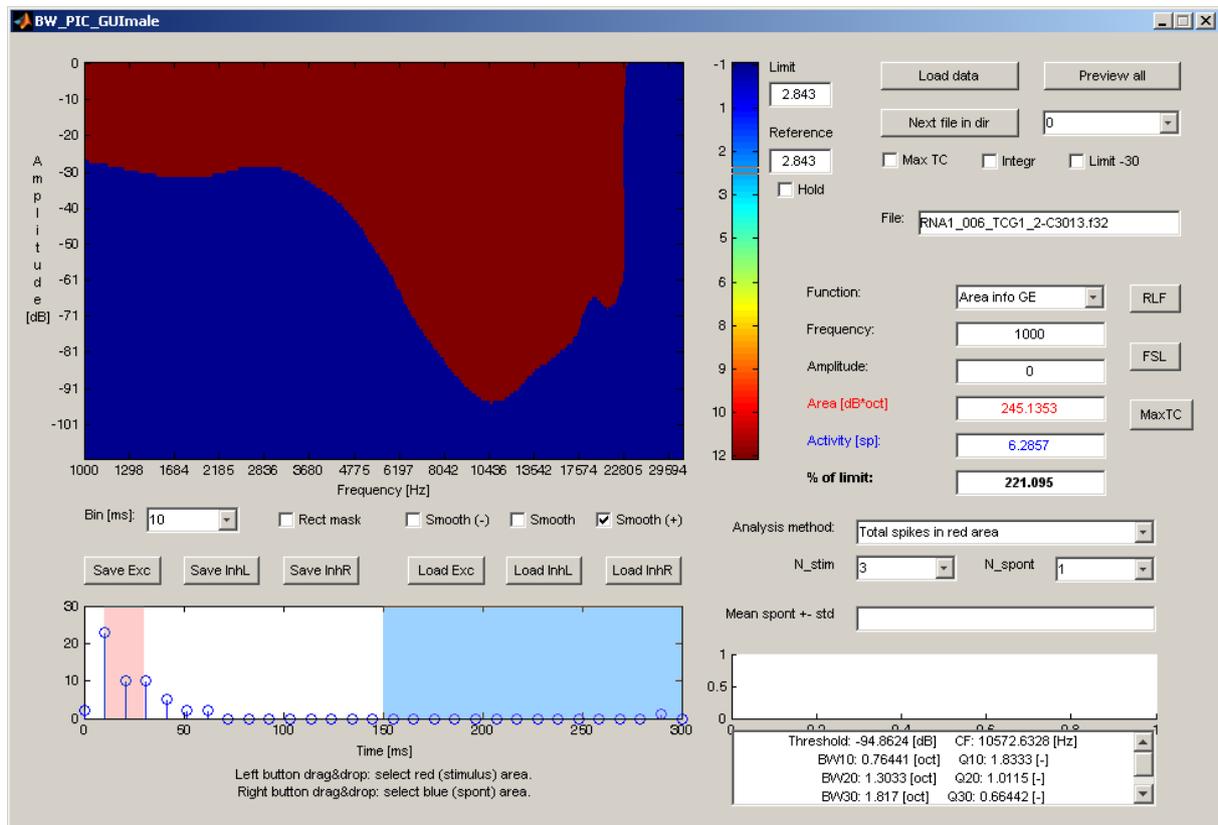


Figure 6: Main window of the graphical user interface. The settings of the FIRA evaluation are set analogously as in Fig. 4. A filled suprathreshold area is shown for the smoothed version of the FIRA.

At the right side of the main window, buttons for loading files are placed; the tool is provided with a function of FIRA preview of up to 16 neurons (opens in a new window), and a possibility of one-click loading of the next data file in the current directory. Below, one of three evaluation functions of the tool may be set:

- “point info”, which shows the information about a selected FIRA point,
- detection of suprathreshold area, used for the extraction of the tuning curve,
- detection of subthreshold area, used for the detection of inhibitory regions.

The threshold used in the latter two functions may be set either by dragging the rectangular marker at the color scale, or, more conveniently, by right-clicking at any point of the FIRA that corresponds to the threshold response magnitude.

At the bottom-right side of the window, control of automated evaluation of suprathreshold area based on the statistics of the evoked and spontaneous activity is placed (see also section Extraction of response parameters). However, during routine utilization of the tool in the neurophysiological practice, the fully automated evaluation of the responses was found to be unsuitable – the evaluation of suboptimal neuronal data often requires higher flexibility which is offered by the manual mode.

At the very right side of the window, buttons for evaluation of RIF, first-spike latency, and overall maximum response magnitude are placed.

5 Data output

Many of the parameters extracted from a FIRA are shown in the main window. However, manual copying of data to a database or a spreadsheet would be annoying and highly inefficient. For this reason, the most common evaluation modes (extraction of tuning curve, RIF, first-spike latency,

and overall maximum response magnitude) are provided with an automated output of the parameters to a tab-separated text file from which the data may be easily imported to any database or spreadsheet. At the same time, the data are copied to the clipboard. The feature of automated data output markedly increased the efficacy of data evaluation.

6 Conclusions

The presented MATLAB tool represents a custom software solution that fulfills all the requirements on FIRA evaluation given by routine neurophysiological practice of the Department of Auditory Neuroscience at the Institute of Experimental Medicine of AS CR. Thanks to this tool, evaluation of the data is more precise and the time needed for the experiment is reduced. Thanks to partially automated and one-click functioning of the tool, the time needed for evaluation of the recorded data was cut down to absolute minimum; for example, evaluation of a tuning curve of one neuron is performed merely by three mouse clicks.

The work was supported by the projects "Podpora a individuální rozvoj perspektivních akademických pracovníků na VŠPJ" at the College Of Polytechnics Jihlava and GAČR 309/07/1336 at the AS CR Prague.

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