QPPLab: A generally applicable software package for detecting, analyzing, and visualizing large-scale quasiperiodic spatiotemporal patterns (QPPs) of brain activity

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Abstract

Quasi-periodic patterns (QPPs) are prominent spatiotemporal brain dynamics observed in functional neuroimaging data, reflecting the alternation of high and low activity across brain regions and their propagation along cortical gradients. QPPs have been linked to neural processes such as attention, arousal fluctuations, and cognitive function. Despite their significance, existing QPP analysis tools are limited by study-specific parameters and complex workflows. To address these challenges, we present ***QPPLab***, an open-source MATLAB-based toolbox for detecting, analyzing, and visualizing QPPs from fMRI time series. QPPLab integrates correlation-based iterative algorithms, supports customizable parameter settings, and features automated workflows to simplify analysis. Processing times vary depending on dataset size and the selected mode, with the fast detection mode completing analyses that can be 4–6 times faster than the robust detection mode. Results include spatiotemporal templates of QPPs, sliding correlation time courses, and functional connectivity maps. By reducing manual parameter adjustments and providing user-friendly tools, QPPLab enables researchers to efficiently study QPPs across diverse datasets and species, advancing our understanding of intrinsic brain dynamics.

Keywords

Infraslow activity, quasiperiodic patterns, spatiotemporal brain dynamics, functional MRI

Metadata

Nr	Code metadata description	
C1	Current code version	v1.0.0
C2	Permanent link to code/repository used for this code version	https://github.com/GT-EmoryMINDlab/QPPLab
C3	Permanent link to reproducible capsule	N/A
C4	Legal code license	MIT License
C5	Code versioning system used	Git
C6	Software code languages, tools and services used	MATLAB
C7	Compilation requirements, operating environments and dependencies	MATLAB R2018 or a later version
C8	If available, link to developer documentation/manual	https://github.com/GT-EmoryMINDlab/QPPLab/blob/main/README.md
C9	Support email for questions	im.nan.xu@gmail.com

1. Motivation and significance

Research on infraslow BOLD fluctuations has significantly advanced our understanding of the brain's functional architecture and its variations during tasks, development, and diseases [1]. Central to these findings is a class of spatiotemporal dynamic patterns known as quasi-periodic patterns (QPPs). QPPs are characterized by alternating high and low activity across brain regions and their propagation along cortical gradients. These patterns, observed in both rodents [2], [3], [4], [5], [6], [7], [8] and humans [4], [9], [10], [11], [12], provide critical insights into functional brain dynamics. Multiple QPPs have been detected [9], [12], with the primary QPP, referred to as QPP1, exhibiting a pronounced anticorrelation between the default mode and task-positive networks across species. Linked to infraslow neural activity [5], [13], QPP1 is influenced by factors like sustained attention [14], memory tasks [14], [15], and arousal fluctuations [10].

The detection and analysis of QPPs have evolved over time. An initial detection algorithm for QPP1 was introduced by [4] for fMRI data from brain voxels using correlation-based and iterative methods to identify similar segments in functional timecourses to create a spatiotemporal template [2], [3], [4]. This algorithm, widely adopted in rodent and human studies, was later tailored for fMRI data extracted from the Brainnetome [15] and Glasser [12], [16] atlases. These adaptations enabled the observation of region-of-interest (ROI) and network-based QPPs throughout the human brain. Recently, [12] introduced an enhanced algorithm that capable of detecting not only QPP1 but also additional patterns, such as QPP2 and QPP3, in humans. By regressing QPP1 from the data and applying iterative techniques to the residuals, these methods have revealed new insights into brain connectivity patterns.

Despite these advances, existing tools for QPP analysis face significant limitations. Traditional methods heavily depend on study-specific settings, including predefined atlas schemes [12], [15], specific brain regions [4], particular species [2], [3], [7], [8], or an exclusive focus on QPP1s [15], [16]. This dependence not only restricts their versatility but also complicates the user experience with redundant parameters, increasing the potential for errors and inconsistencies.

Recognizing these limitations, we developed *QPPLab*, an open-source MATLAB package specifically designed to analyze QPPs. QPPLab provides a streamlined, user-friendly, and robust tool for detecting, analyzing, and interpreting these spatiotemporal patterns. The toolbox introduces several key advancements:

1. **Automation**: QPPLab automates parameter selection and workflow execution, minimizing manual intervention and simplifying the analysis process.
2. **Multiple Detection Modes**: Users can choose between fast and robust detection modes to balance speed and accuracy based on their research needs.
3. **Expanded Analytical Capabilities**: QPPLab supports additional analyses, including functional connectivity computation after QPP regression and phase-adjusted QPP visualization.
4. **Broad Applicability**: Unlike traditional methods, QPPLab is designed to handle diverse datasets and species, making it a universally applicable tool.

5. **Streamlined Workflow**: QPPLab integrates advanced correlation-based iterative algorithms into a cohesive platform, ensuring reproducibility and efficiency.

By overcoming the limitations of traditional tools and reducing the need for manual, study-specific parameter adjustments, QPPLab enables researchers to efficiently study intrinsic brain dynamics across diverse datasets and experimental contexts [6], [17], [18]. This innovation represents a significant advancement in our understanding of functional brain dynamics and connectivity.

2. Software description

QPPLab was modified and expanded based on the latest QPP analytic tools [12], which can detect, analyse, and visualize QPP1 as well as additional QPPs from functional neuroimaging timeseries of the brain. This software also encompasses analytical and visualization techniques introduced in [4], [6], [12], [15], [16].

The main QPP detection algorithm [4] and its two major outputs are described in Fig. 1. In brief, a 4-step procedure was performed: 1) an initial segment with a fixed window length is selected at a random starting point from the functional timecourse; 2) this selected segment is correlated with a segment with the same window length that is sliding from the beginning to the end of the timecourse at every timepoint, which results in a timecourse of sliding correlation values; 3) the segments, that are corresponding to the local maxima of the correlation timecourse, are then averaged to obtain the new segment; 4) steps 2-3 are iterated until the averaged segment and the selected segment converge.

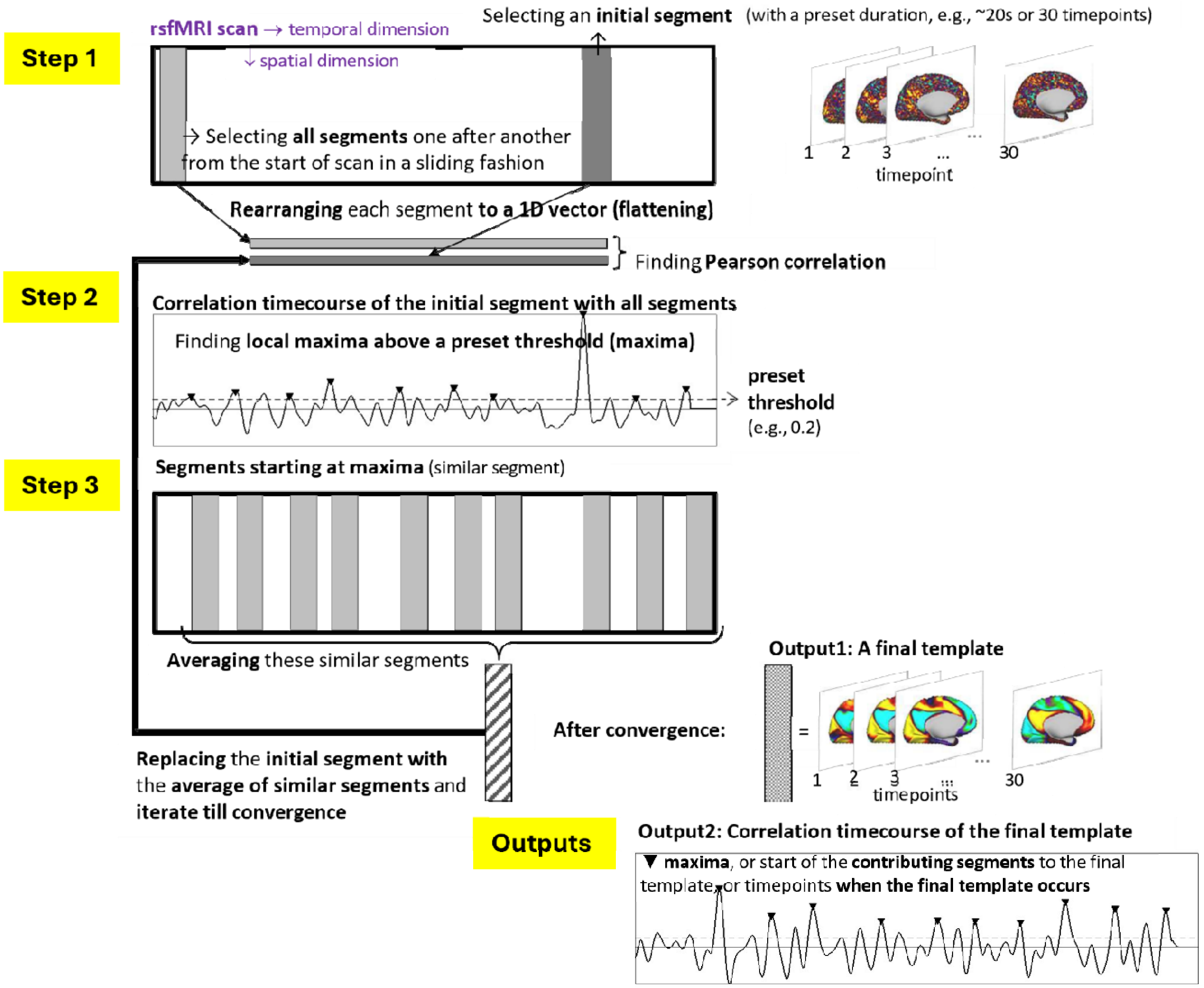

Step 1
rsfMRI scan → temporal dimension
↓ spatial dimension
Selecting an initial segment (with a preset duration, e.g., ~20s or 30 timepoints)
→ Selecting all segments one after another from the start of scan in a sliding fashion
1
2
3
...
30
timepoint
Rearranging each segment to a 1D vector (flattening)
Finding Pearson correlation
Step 2
Correlation timecourse of the initial segment with all segments
Finding local maxima above a preset threshold (maxima)
preset threshold (e.g., 0.2)
Step 3
Segments starting at maxima (similar segment)
Averaging these similar segments
Replacing the initial segment with the average of similar segments and iterate till convergence
After convergence:
Output1: A final template
=
1
2
3
...
30
timepoints
Outputs
Output2: Correlation timecourse of the final template
▼ maxima, or start of the contributing segments to the final template, or timepoints when the final template occurs

Figure 1 QPP detection algorithm and its output format (adapted from [12], Fig. S2). The output of QPP includes a) a final template of QPP and b) a correlation timecourse of the final template.

Based on the approach introduced in [12], *QPPLab* includes an extended version of this detection algorithm. Specifically, multiple initial segments are selected, and the 4-step procedure is performed for each selection. The averaged QPP with the greatest summation of local maxima of sliding correlations will be selected as the final template.

QPPLab provides two operation modes: a fast detection and a robust detection. The fast mode randomly selects a subset of initial segments from the timecourse e.g., [4], [16], whereas the robust mode evaluates all potential segments, e.g., [6], [12]. This dual-mode approach offers flexibility based on research requirements. Furthermore, *QPPLab* allows users to exclude undesirable timepoints in fMRI data, ensuring QPP results aren't skewed by motion distortions or other artifacts.

Notably, *QPPLab* utilizes an algorithm based on correlation and regressions, and can identify multiple spatiotemporal patterns. These spatiotemporal are analogous to the spatiotemporal patterns delineated by a sophisticated principal component analysis approach [9]. For instance, in the absence of the application of global signal regression to the BOLD signals, QPP1-3 would roughly mirror the patterns 1-3 discovered in [9].

2.1. Software architecture*:*

Below is an overview of the software architecture:

2.1.1. Prerequisites:

- Software Dependencies: The package requires MATLAB (The MathWorks Inc., Natick, MA, USA, R2018a or a later version) to run. All necessary MATLAB functions and source code required to execute the pipeline are provided in the ./src/ folder.
- Input Data: The package operates on functional neuroimaging data stored in the ./data/data.mat file. This file needs to include several input variables such as D0, MotionInf, ROI2Net, and NetLB (see Table 1) that are necessary for analysis.

Input variables	Description	Note
D0	a (nsbj X nscn) cell matrix	Each cell has a (nroi X ntimepoints) matrix of EPI timeseries.
MotionInf	a (nsbj X nscn) cell matrix	Each cell includes >=1 segment(s) of timepoints selected for the QPP detection. Timepoints with motion or artifacts can be excluded.
ROI2Net	a (nroi X 1) vector	Each entry is the network index corresponding to each ROI.
NetLB	a (nnet X 1) cell vector	Each cell includes the (shorthand) label of each network.

Table 1: Input variables. nsbj= number of subjects, nscn=number of EPI scans, nroi=number of ROIs, ntimepoints=number of timepoints, nnet= number of networks.

Note that the ROI2Net and NetLB variables can be generated from your atlas-network file stored in the ./asseour original input file; if you did not prepare the MotionInf parameter, the entire timepoints of each scan will be included in MotionInf when running 'st0_ROIreOrg.m'.

2.1.2. Main Pipeline:

The main pipeline consists of three steps, with each step's script included in the ./src/ folder:

- Step 1: Setting Parameters (st1_ParamsSet.m): Setting Parameters (st1_ParamsSet.m): In this step, global analysis parameters are specified, divided into sections like file paths, QPP global/detection/phase adjustment parameters, and functional connectivity analysis parameters. These settings shape the pipeline's following stages. A detailed overview of these parameters, apart from file paths, can be found in Table 2. For a deeper dive into each parameter, see the table in Section 2.1 of the README manual.

Category	Parameter	Description
QPP global parameters	nP	total number of QPPs to detect
	PL	QPP window length
QPP detection parameters	cth13 & cth45	correlation threshold for different QPPs
QPP phase adjustment	Cthph	similarity threshold when phase-adjusting a QPP

parameters	S	control for strict or relaxed phase adjustment
	Sdph	reference parcels
Functional connectivity (FC) analysis parameters	Fz	control the output FC map to either use Pearson correlation or its Fisher Z-Transformation

Table 2 Global parameters setup in 'st1_ParamsSet.m'

- Step 2: QPP Analysis (st2_QPPanalysis.m): In this step, QPP analysis is executed using parameters from Step 1. The script detects QPPs, performs phase adjustment, detects additional QPPs from residuals, and computes functional connectivity after QPP regression. Key outputs include QPP templates, correlation timelines, and functional connectivity maps.
- Step 3: Visualization (st3_QPPFCvisual.m): The final step involves visualizing the results of the QPP analysis. This script generates various figures illustrating the detected QPPs, their phase-reversed counterparts, sliding correlation timecourses and their histograms, as well as functional connectivity matrices before and after QPP regression. The script takes parameters for specifying which QPPs and groups to visualize.

2.1.3. Output Files:

The output files are organized into directories corresponding to the type of analysis conducted (GrpQPP, SbjQPP, ScnQPP), all located within the ./results/ folder. Output files include intermediate results as well as key output variables generated during the QPP analysis and visualization steps (described in Section 2.2.2 in the README manual). These variables provide information about detected QPPs, their characteristics, and the results of various analyses. Examples of output files saved by different parameter settings are described in section 3 in the README manual.

2.2. Key functions of QPP analysis*:*

The computational framework implemented in the script st2_QPPanalysis.m encompasses a sequence of five analytical procedures designed to extract QPPs and related results present in the data. These five procedures are outlined below.

- *QPP1 Detection:* The initial phase involves the identification of the primary Quasi-Periodic Pattern 1 (QPP1), an intrinsic dynamic phenomenon in the brain. Leveraging the algorithm developed by [4] and subsequently enhanced by [12], this step utilizes a correlation-based approach to detect and separate these phase-locked patterns within a series of chosen timecourses from the brain regions under study. The chosen timecourses are specified in MotionInf as detailed in Table 1.
- *Phase Adjustment*: Based on the findings of [12], this stage involves precise phase adjustments to synchronize the phases of QPP1 consistently across all brain regions. During this process, a reference brain region is selected, of which QPP waveform begins from a positive value. This intricate synchronization enhances the comparability of multiple QPPs (e.g., QPP1, QPP2, QPP3, etc.) within a given population.
- *Detection of Additional QPPs (optional):* Extending the analytical framework presented by [12], this computation explores residual data following QPP1 regression. The detection of secondary (and potentially tertiary) QPPs from these residuals provides a

more comprehensive exploration of this phase-locked intrinsic dynamic process. Parameters for the detection of additional QPPs can be defined within st1_QPPparam.m.

- *Reverse Phase QPP Detection:* Introduced by [6], this step identifies QPPs in their reverse phase. For each QPP, a counterpart in reverse phase is identified. This reverse phase QPP is derived by averaging segments that initiate from the local minima of the identical correlation timecourse employed to extract the original QPP in either step 1 or 3. This reverse QPP assists in facilitating comparisons due to the half-wave symmetric nature of QPPs as described in [6].
- *Functional Connectivity Computation after QPP Regression*: Building upon the frameworks of [6], [12], [15], this final computation computes the functional connectivity (FC) map from the residue after the QPP regression. By systematically removing QPP-related signals, this analysis unveils refined functional connectivity patterns, implicating the amount of FC contributed by QPPs.

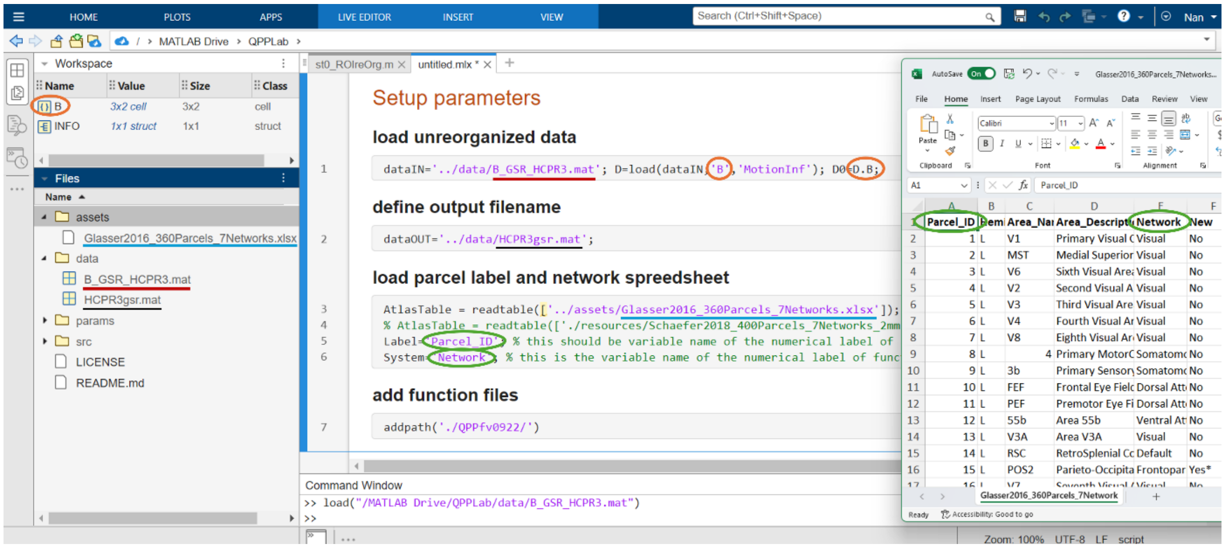
These computations collectively offer a comprehensive toolkit to study QPPs and their contributions in brain functional connectivity. By integrating established methodologies, this analytical framework contributes to advancing our understanding of the intricate spatiotemporal dynamics within the brain data.

3. Illustrative example

This toolbox has been demonstrated on various datasets with different atlas schemes. Including resting and task human fMRI dataset [6], [19] as well as multiple rodent fMRI datasets [6]. One illustrative example of resting fMRI Human Connectome Project (HCP) data extracted from Glasser atlas [20] is provided in this section.

3.1. Prepare the input file

The initial input file should contain a cell matrix of EPI timeseries with dimensions (nsbj X nscn), which can be represented as 'B' in the file './data/B_GSR_HCPR3.mat'. If the remaining variables (MotionInf, ROI2Net, and NetLB) haven not been prepared beforehand, they can be created using the 'st0_ROIreOrg.m' script in the ./src/ folder. Specifically, the user needs to specify parameters in the script's initial three sections, as illustrated in Figure 1. Note that the atlas spreadsheet (highlighted with blue underscores in Figure 1) must encompass ROI labels and their corresponding functional networks (green circles in Figure 2).



Name	Value	Size	Class
B	3x2 cell	3x2	cell
INFO	1x1 struct	1x1	struct

Setup parameters

load unreorganized data

```
dataIN='../data/B_GSR_HCPR3.mat'; D=load(dataIN,'B','MotionInf'); D0=D.B;
```

define output filename

```
dataOUT='../data/HCPR3gsr.mat';
```

load parcel label and network spreedsheet

```
AtlasTable = readtable(['../assets/Glasser2016_360Parcels_7Networks.xlsx']);
% AtlasTable = readtable(['./resources/Schaefer2018_400Parcels_7Networks_2mm
Label='Parcel_ID'; % this should be variable name of the numerical label of
System='Network'; % this is the variable name of the numerical label of func
```

add function files

```
addpath('./QPPfv0922/')
```

Command Window

```
>> load("/MATLAB Drive/QPPLab/data/B_GSR_HCPR3.mat")
>>
```

	A	B	C	D	E	F
1	Parcel_ID	Hemi	Area_Nai	Area_Descripti	Network	New
2	1	L	V1	Primary Visual C	Visual	No
3	2	L	MST	Medial Superior	Visual	No
4	3	L	V6	Sixth Visual Area	Visual	No
5	4	L	V2	Second Visual A	Visual	No
6	5	L	V3	Third Visual Are	Visual	No
7	6	L	V4	Fourth Visual Ar	Visual	No
8	7	L	V8	Eighth Visual Ar	Visual	No
9	8	L	4	Primary MotorC	Somatomc	No
10	9	L	3b	Primary Sensory	Somatomc	No
11	10	L	FEF	Frontal Eye Fielc	Dorsal Att	No
12	11	L	PEF	Premotor Eye Fi	Dorsal Att	No
13	12	L	55b	Area 55b	Ventral At	No
14	13	L	V3A	Area V3A	Visual	No
15	14	L	RSC	RetroSplenial Cc	Default	No
16	15	L	POS2	Parieto-Occipita	Frontopar	Yes*
17	16	L	V7	Seventh Visual (	Visual	No

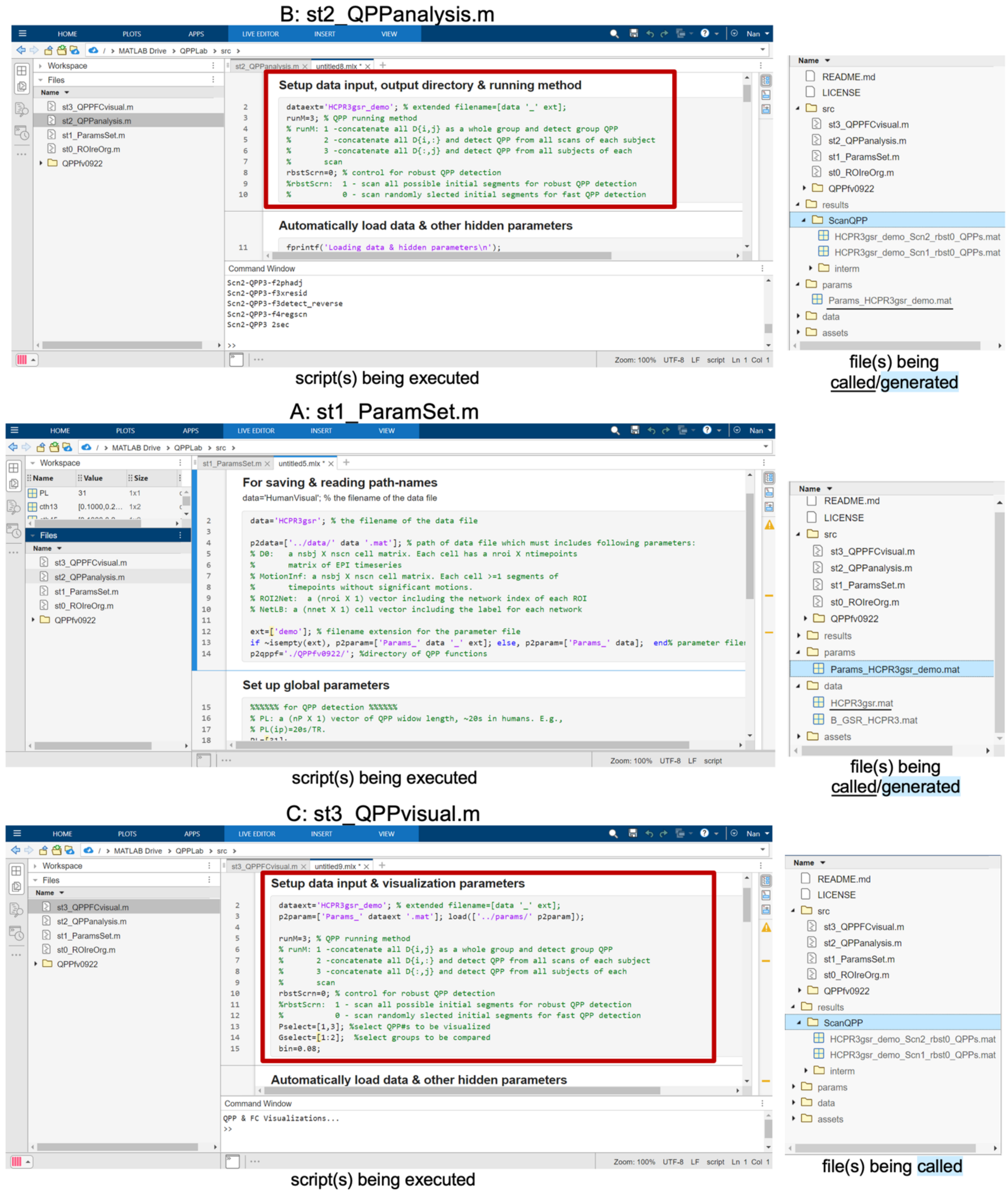
Figure 2 Input variables generation.

3.2. Configuring parameters for QPP analysis and visualization

After preparing the input file, users will run the ‘st1_ParamSet.m’ script in the ./src/ folder to define parameters and thresholds for QPP detection, phase adjustment, and network analysis. Each parameter's role is explained in the script's comments and further detailed in the README manual. On executing 'st1_ParamSet.m', parameters are adjusted based on user preferences and data characteristics. For instance, with an input file named 'HCPR3gsr' (a file obtained by 'st0_ROIreOrg.m'), parameters will be saved as 'Param_HCPR3gsr_demo.mat' in the ./params/ folder, showcased in Figure 3A.

Next, the user proceeds to execute the script named 'st2_QPPanalysis.m' to perform the QPP analysis. When running this script, the user's focus is directed solely to the first section, where they can select operational preferences. This is highlighted by a red square in Figure 3B. All resulting output files will be preserved in the designated ./results/ directory.

Finally, the user will execute the script 'st3_QPPvisual.m' to visualize QPP(s) and associated results saved in the ./results/ directory. When running this script, the user still focuses the first section for operational choices (highlighted by a red square in Figure 3C). Note that the operational choices selected in this section and the ones in 'st2_QPPanalysis.m' must be consistent.



B: st2_QPPanalysis.m

Setup data input, output directory & running method

```
dataext='HCPR3gsr_demo'; % extended filename=[data '_' ext];
runM=3; % QPP running method
% runM: 1 -concatenate all D{i,j} as a whole group and detect group QPP
%       2 -concatenate all D{i,:} and detect QPP from all scans of each subject
%       3 -concatenate all D{:,j} and detect QPP from all subjects of each
%       scan
rbstScrn=0; % control for robust QPP detection
%rbstScrn:  1 - scan all possible initial segments for robust QPP detection
%           0 - scan randomly slected initial segments for fast QPP detection
```

Automatically load data & other hidden parameters

```
fprintf('Loading data & hidden parameters\n');
```

Command Window

```
Scn2-QPP3-f2phadj
Scn2-QPP3-f3xresid
Scn2-QPP3-f3detect_reverse
Scn2-QPP3-f4regscn
Scn2-QPP3 2sec
>>
```

script(s) being executed

file(s) being called/generated

A: st1_ParamSet.m

For saving & reading path-names

data='HumanVisual'; % the filename of the data file

```
data='HCPR3gsr'; % the filename of the data file

p2data=['../data/' data '.mat']; % path of data file which must includes following parameters:
% D0:    a nsbj X nscn cell matrix. Each cell has a nroi X ntimepoints
%        matrix of EPI timeseries
% MotionInf: a nsbj X nscn cell matrix. Each cell >=1 segments of
%        timepoints without significant motions.
% ROI2Net:  a (nroi X 1) vector including the network index of each ROI
% NetLB: a (nnet X 1) cell vector including the label for each network

ext=['demo']; % filename extension for the parameter file
if ~isempty(ext), p2param=['Params_' data '_' ext]; else, p2param=['Params_' data];  end% parameter file
p2qppf='./QPPfv0922/'; %directory of QPP functions
```

Set up global parameters

```
%%%%%% for QPP detection %%%%%%
% PL: a (nP X 1) vector of QPP widow length, ~20s in humans. E.g.,
% PL(ip)=20s/TR.
```

script(s) being executed

file(s) being called/generated

C: st3_QPPvisual.m

Setup data input & visualization parameters

```
dataext='HCPR3gsr_demo'; % extended filename=[data '_' ext];
p2param=['Params_' dataext '.mat']; load(['../params/' p2param]);

runM=3; % QPP running method
% runM: 1 -concatenate all D{i,j} as a whole group and detect group QPP
%       2 -concatenate all D{i,:} and detect QPP from all scans of each subject
%       3 -concatenate all D{:,j} and detect QPP from all subjects of each
%       scan
rbstScrn=0; % control for robust QPP detection
%rbstScrn:  1 - scan all possible initial segments for robust QPP detection
%           0 - scan randomly slected initial segments for fast QPP detection
Pselect=[1,3]; %select QPP#s to be visualized
Gselect=[1:2];  %select groups to be compared
bin=0.08;
```

Automatically load data & other hidden parameters

Command Window

```
QPP & FC Visualizations...
>>
```

script(s) being executed

file(s) being called

Figure 3 Parameter configurations for QPP analysis and visualization.

3.3. Visualization of results

The script will automatically produce six distinct figures, each designed for a specific purpose, which includes 1) A visualization depicting the detected Quasi-Periodic Patterns (QPPs); 2) the phase-reversed counterparts of the QPPs that were identified; 3) sliding correlation timecourse depicting the initiation point of the ongoing QPPs.; 4) sliding correlation timecourses between QPP and the whole scan before and after undergoing the QPP regression; 5) histograms portraying the distribution of these sliding correlation timecourses; 6) functional connectivity matrices showcased both before and after the application of QPP regression (see Figure 4).

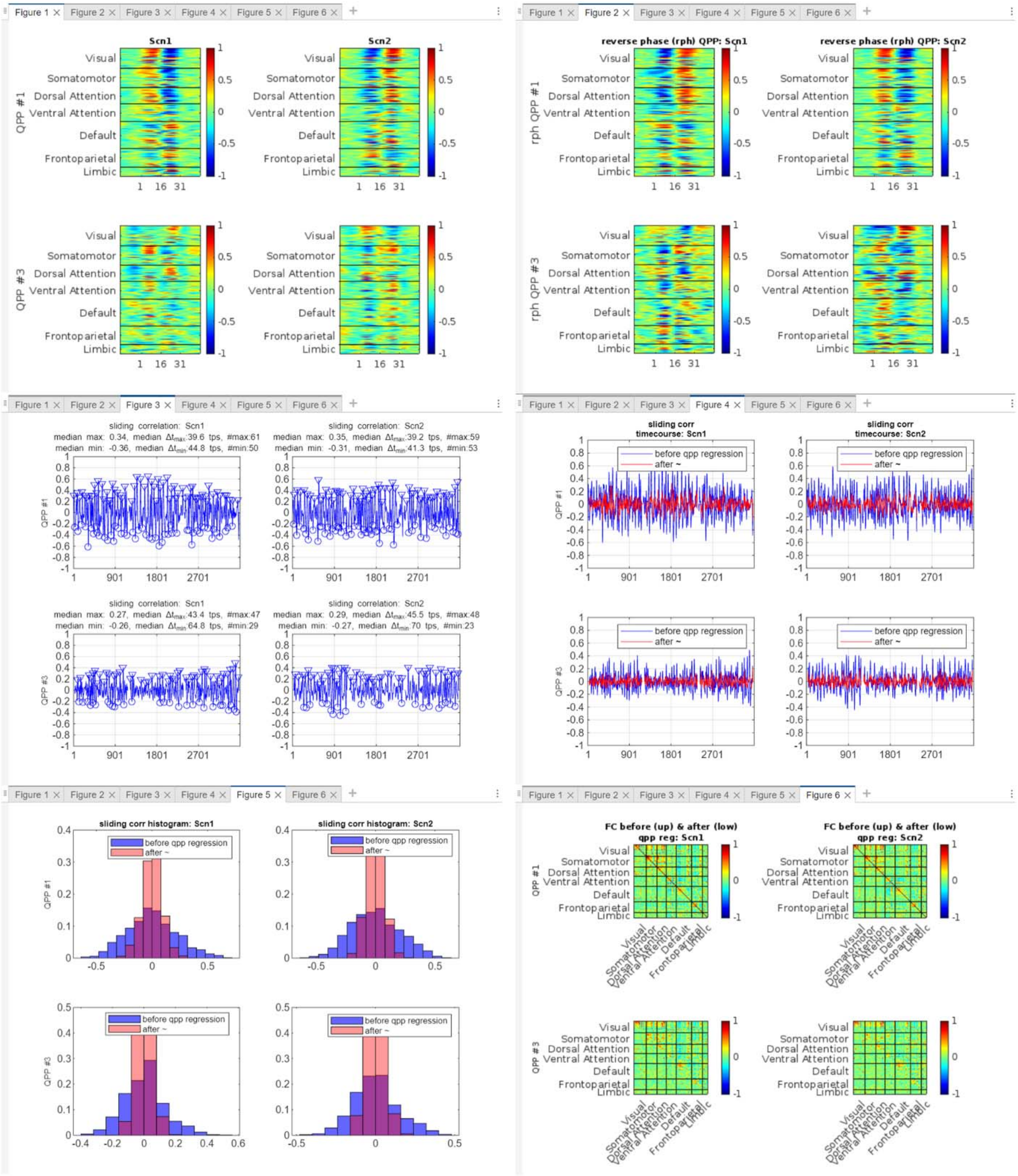


Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
Scn1
Scn2
QPP #1
QPP #3
Visual
Somatomotor
Dorsal Attention
Ventral Attention
Default
Frontoparietal
Limbic
1 16 31
1
0.5
0
-0.5
-1
reverse phase (rph) QPP: Scn1
reverse phase (rph) QPP: Scn2
rph QPP #1
rph QPP #3
sliding correlation: Scn1
median max: 0.34, median Δtmax:39.6 tps, #max:61
median min: -0.36, median Δtmin:44.8 tps, #min:50
sliding correlation: Scn2
median max: 0.35, median Δtmax:39.2 tps, #max:59
median min: -0.31, median Δtmin:41.3 tps, #min:53
sliding correlation: Scn1
median max: 0.27, median Δtmax:43.4 tps, #max:47
median min: -0.26, median Δtmin:64.8 tps, #min:29
sliding correlation: Scn2
median max: 0.29, median Δtmax:45.5 tps, #max:48
median min: -0.27, median Δtmin:70 tps, #min:23
1 901 1801 2701
sliding corr timecourse: Scn1
sliding corr timecourse: Scn2
before qpp regression
after ~
sliding corr histogram: Scn1
sliding corr histogram: Scn2
FC before (up) & after (low) qpp reg: Scn1
FC before (up) & after (low) qpp reg: Scn2

Figure 4 Six figures generated automatically by the script 'st3_QPPvisual.m'. As an example, these figures show the output from resting fMRI HCP data of two concatenated scans (`runM=3`), each encompassing three subjects. Global signal

regression was applied to the data in preprocessing. The algorithm utilized a window length of 22.32s (PL=31 TRs). Three QPPs (QPP1, QPP2, and QPP3) were detected for each scan. However, only the results for QPP1 and QPP3 are depicted in the figures.

Additionally, users can swiftly visualize the phase-adjusted QPPs or the network-specific QPP waveforms using the command line, as demonstrated in Figure 5, facilitating deeper analysis.

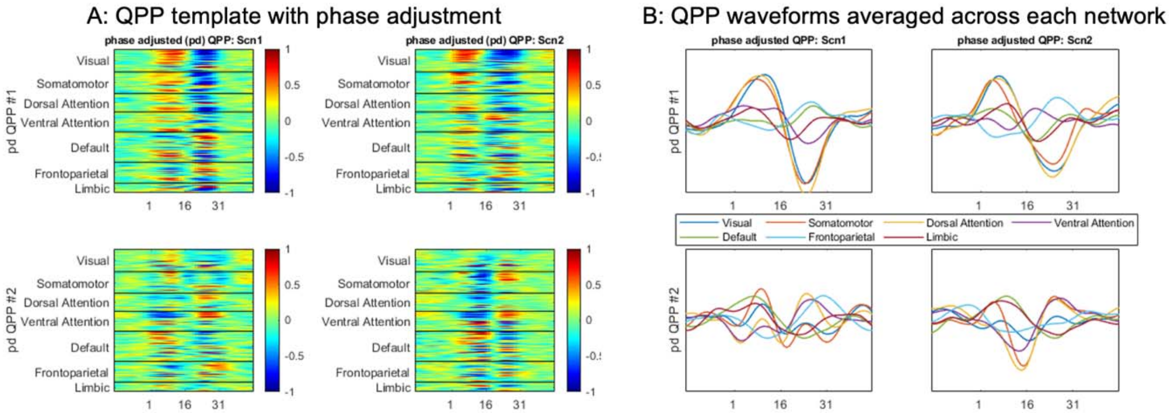


Figure 5 QPPs with adjusted phases. A: the primary and secondary QPP following phase adjustments. In each sub-figure, the QPP of the `ip`-th order, whose phase is aligned based on the `is`-th seed, is displayed using the command: `imagesc(QPPas{ip}{is}(iROI2Net,:),[-1 1]);` B: Averaged QPP waveforms across networks for the primary and secondary QPPs with phase adjustments. In every sub-figure, the averaged QPP waveform for the `inet`-th network is illustrated using the command: `plot(mean(QPPas{ip}{2}(find(ROI2Net==inet),:)',2));`

3.4. Comparison between fast QPP detection and robust QPP detection

As described in the 4th paragraph of Section 2, QPPLab supports two operation modes through the ‘`rbstScrn`’ flag in the script 'st2_QPPanalysis.m': a fast detection mode (`rbstScrn=0`) that randomly selects a subset of initial segments, potentially leading to slightly different sets of detected QPPs across different runs, as illustrated in Figure 6. Conversely, the robust detection mode (`rbstScrn=1`) evaluates all potential segments to derive the global optimal QPP results (Figure 6). The execution time across fast and robust mode of QPP detection is shown in Table 1. Previous work has employed both fast mode (e.g., [2], [3], [4], [5], [10], [15], [16]) and robust mode ([6], [12], [19], [21]). While fast mode yields much quicker results, robust mode is highly preferred for accurate QPP detection, particularly in individual-level or small-group analyses.

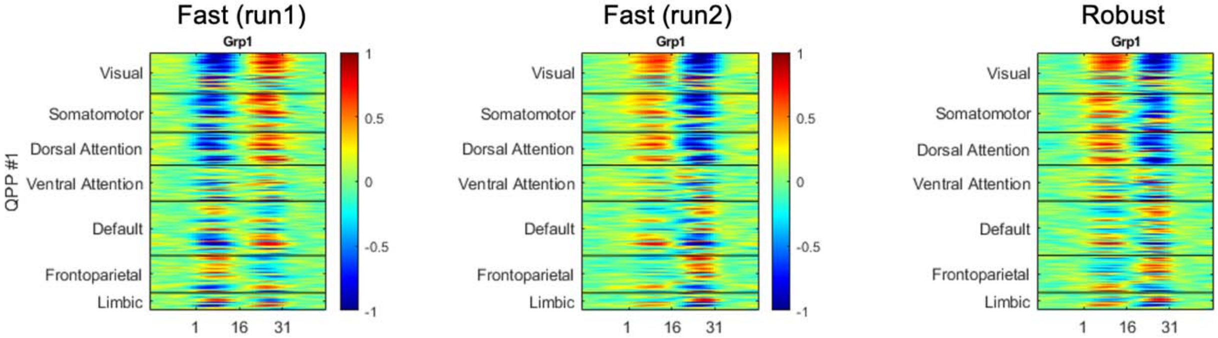


Figure 6 QPP comparison across different operation modes. These figures show the primary QPP detected from all concatenated scans (`runM=1`). Two runs of the fast detection mode (`rbstScrn=0`) and one run of the robust detection mode are shown.

QPP detection mode	2400 tps	3600 tps	7200 tps
Fast (run1)	6s	13s	62s
Fast (run2)	5s	14s	60s
Robust	38s	82s	283s

Table 1: execution time of QPP detection across different operation modes. The robust detection mode was compared with two runs of the fast detection mode across three different time courses with 2400, 3600, and 7200 time points, respectively. The software was executed on a CPU @ 2.1GHz (2 processors, 768GB RAM), utilizing 48 cores for parallel computing.

4. Impact

QPPLab is an open-source MATLAB software package, which offers a comprehensive toolset for researchers to study the quasiperiodic spatiotemporal BOLD dynamics for any dataset. This software introduces several avenues for advancing neuroscience and neuroimaging research and addressing important questions in the field.

Advancing Research Frontiers: By offering a user-friendly interface and standardized methodologies, QPPLab empowers researchers to explore QPPs in any fMRI dataset. With QPPs playing a pivotal role in attention [14], [15] and arousal fluctuations [10], as well as in disorders such as ADHD [14] and Alzheimer's Disease [3] across both rodents and humans, this software suite presents a platform to delve into new research inquiries concerning intrinsic spatiotemporal dynamics under novel circumstances. Researchers are empowered to investigate the fundamental mechanisms driving functional connectivity, their contribution in diverse cognitive functions, and brain disorders.

Changing Common Practices: QPPLab offers unprecedented capabilities for QPP analysis by integrating multiple established algorithms and analytical techniques. This standardization enhances reproducibility and reliability, allowing researchers to quantitatively assess how QPPs differ from one another and their contributions to functional connectivity. These insights are vital for understanding the brain’s intrinsic dynamic patterns and their functional significance.

Improving Research Rigor: QPPLab provides an accessible and user-friendly platform that reduces the technical barriers posed by previous study-specific algorithms. Its parameter-simplified toolbox streamlines QPP analysis across diverse datasets, enabling researchers to investigate the reproducibility and consistency of QPPs across species and brain regions. This approach sheds light on fundamental principles of brain organization. Published studies utilizing *QPPLab* [6], [17], [18] have enhanced the precision and accuracy of QPP detection and analysis, leading to a deeper understanding of brain function.

5. Conclusions

We have introduced *QPPLab*, an open-source MATLAB software package designed to detect, analyze, and visualize QPPs and related results from functional neuroimaging time series. QPPLab integrates established methods into an enhanced algorithm and user-friendly interface, providing a streamlined workflow for QPP analysis. This software represents a significant advancement in the study of functional brain dynamics by enabling rigorous investigations with minimal manual intervention. Its automation, ability to detect multiple QPPs, and support for reproducible research open new avenues for exploring cognitive processes and neurological disorders across humans and other species. QPPLab's comprehensive features position it as a critical tool for advancing neuroscience and understanding the brain's intrinsic dynamic patterns.

Acknowledgments

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References

[1] M. D. Fox and M. E. Raichle, “Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging,” *Nature Reviews Neuroscience 2007 8:9*, vol. 8, no. 9, pp. 700–711, Sep. 2007, doi: 10.1038/nrn2201.

[2] M. E. Belloy *et al.*, “Dynamic resting state fMRI analysis in mice reveals a set of Quasi-Periodic Patterns and illustrates their relationship with the global signal,” Oct. 15, 2018, *Academic Press Inc.* doi: 10.1016/j.neuroimage.2018.01.075.

[3] M. E. Belloy *et al.*, “Quasi-Periodic Patterns of Neural Activity improve Classification of Alzheimer's Disease in Mice,” *Sci Rep*, vol. 8, no. 1, p. 10024, Dec. 2018, doi: 10.1038/s41598-018-28237-9.

[4] W. Majeed *et al.*, “Spatiotemporal dynamics of low frequency BOLD fluctuations in rats and humans,” *Neuroimage*, vol. 54, no. 2, pp. 1140–1150, 2011, doi: 10.1016/j.neuroimage.2010.08.030.

[5] G. J. Thompson, W. J. Pan, M. E. Magnuson, D. Jaeger, and S. D. Keilholz, “Quasi-periodic patterns (QPP): Large-scale dynamics in resting state fMRI that correlate with local infraslow electrical activity,” *Neuroimage*, vol. 84, pp. 1018–1031, Jan. 2014, doi: 10.1016/j.neuroimage.2013.09.029.

[6] N. Xu, D. M. Smith, G. Jeno, D. T. Seeburger, E. H. Schumacher, and S. D. Keilholz, “The interaction between random and systematic visual stimulation and infraslow quasi-periodic spatiotemporal patterns of whole-brain activity,” *Imaging Neuroscience*, vol. 1, pp. 1–19, Sep. 2023, doi: 10.1162/IMAG_A_00002.

[7] N. Anumba *et al.*, “The effects of locus coeruleus optogenetic stimulation on global spatiotemporal patterns in rats,” *Imaging Neuroscience*, vol. 2, pp. 1–20, Dec. 2024, doi: 10.1162/IMAG_A_00314.

[8] L. Meyer-Baese *et al.*, “Variation in the distribution of large-scale spatiotemporal patterns of activity across brain states,” *Front Syst Neurosci*, vol. 18, p. 1425491, Aug. 2024, doi: 10.3389/FNSYS.2024.1425491/BIBTEX.

[9] T. Bolt *et al.*, “A parsimonious description of global functional brain organization in three spatiotemporal patterns,” *Nature Neuroscience 2022 25:8*, vol. 25, no. 8, pp. 1093–1103, Jul. 2022, doi: 10.1038/s41593-022-01118-1.

[10] R. V. Raut *et al.*, “Global waves synchronize the brain’s functional systems with fluctuating arousal,” *Sci Adv*, vol. 7, no. 30, Jul. 2021, doi: 10.1126/SCIADV.ABF2709/SUPPL_FILE/SCIADV.ABF2709_SM.PDF.

[11] N. Xu *et al.*, “Rodent Whole-Brain fMRI Data Preprocessing Toolbox,” *Aperture Neuro*, 2021, Accessed: Nov. 10, 2021. [Online]. Available: https://github.com/GT-EmoryMINDlab/rodent-whole-brain-preprocessing-recipe

[12] B. Yousefi and S. Keilholz, “Propagating patterns of intrinsic activity along macroscale gradients coordinate functional connections across the whole brain,” *Neuroimage*, vol. 231, p. 117827, Feb. 2021, doi: 10.1016/j.neuroimage.2021.117827.

[13] J. K. Grooms *et al.*, “Infraslow Electroencephalographic and Dynamic Resting State Network Activity,” *Brain Connect*, vol. 7, no. 5, p. 265, Jun. 2017, doi: 10.1089/BRAIN.2017.0492.

[14] A. Abbas, Y. Bassil, and S. Keilholz, “Quasi-periodic patterns of brain activity in individuals with attention-deficit/hyperactivity disorder,” *Neuroimage Clin*, vol. 21, p. 101653, Jan. 2019, doi: 10.1016/j.nicl.2019.101653.

[15] A. Abbas *et al.*, “Quasi-periodic patterns contribute to functional connectivity in the brain,” *Neuroimage*, vol. 191, pp. 193–204, May 2019, doi: 10.1016/J.NEUROIMAGE.2019.01.076.

[16] B. Yousefi, J. Shin, E. H. Schumacher, and S. D. Keilholz, “Quasi-periodic patterns of intrinsic brain activity in individuals and their relationship to global signal,” *Neuroimage*, vol. 167, pp. 297–308, Feb. 2018, doi: 10.1016/j.neuroimage.2017.11.043.

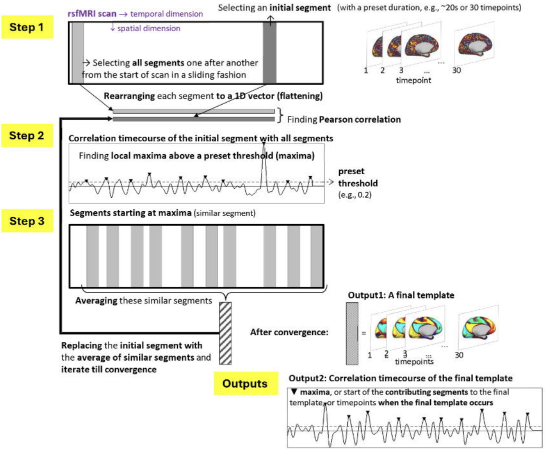
[17] N. Xu *et al.*, “Rodent Whole-Brain fMRI Data Preprocessing Toolbox,” *Aperture Neuro*, pp. 1–3, Aug. 2023, doi: 10.52294/001C.85075.

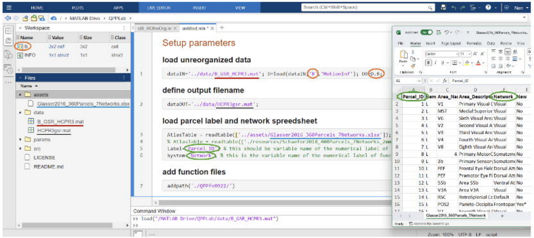
[18] D. T. Seeburger *et al.*, “Time-varying functional connectivity predicts fluctuations in sustained attention in a serial tapping task,” *Cognitive, Affective, & Behavioral Neuroscience 2024 24:1*, vol. 24, no. 1, pp. 111–125, Jan. 2024, doi: 10.3758/S13415-024-01156-1.

[19] D. T. Seeburger *et al.*, “Time-varying Functional Connectivity Predicts Fluctuations in Sustained Attention in a Serial Tapping Task,” *bioRxiv*, p. 2023.06.22.546092, Jun. 2023, doi: 10.1101/2023.06.22.546092.

[20] M. F. Glasser *et al.*, “A multi-modal parcellation of human cerebral cortex,” *Nature 2016 536:7615*, vol. 536, no. 7615, pp. 171–178, Jul. 2016, doi: 10.1038/nature18933.

[21] E. Maltbie, B. Yousefi, X. Zhang, A. Kashyap, and S. Keilholz, “Comparison of Resting-State Functional MRI Methods for Characterizing Brain Dynamics,” *Front Neural Circuits*, vol. 16, Apr. 2022, doi: 10.3389/FNCIR.2022.681544/FULL.


Step 1
rsfMRI scan → temporal dimension
↓ spatial dimension
Selecting an initial segment (with a preset duration, e.g., ~20s or 30 timepoints)
→ Selecting all segments one after another from the start of scan in a sliding fashion
1
2
3
...
30
timepoint
Rearranging each segment to a 1D vector (flattening)
Finding Pearson correlation
Step 2
Correlation timecourse of the initial segment with all segments
Finding local maxima above a preset threshold (maxima)
preset threshold (e.g., 0.2)
Step 3
Segments starting at maxima (similar segment)
Averaging these similar segments
Replacing the initial segment with the average of similar segments and iterate till convergence
Output1: A final template
After convergence:
=
1
2
3
...
30
timepoints
Outputs
Output2: Correlation timecourse of the final template
▼ maxima, or start of the contributing segments to the final template, or timepoints when the final template occurs



Name	Value	Size	Class
B	3x2 cell	3x2	cell
INFO	1x1 struct	1x1	struct

```
Name ▴
▾ assets
    Glasser2016_360Parcels_7Networks.xlsx
▾ data
    B_GSR_HCPR3.mat
    HCPR3gsr.mat
▸ params
▸ src
  LICENSE
  README.md
```

Setup parameters

load unreorganized data

```
dataIN='../data/B_GSR_HCPR3.mat'; D=load(dataIN,'B','MotionInf'); D0=D.B;
```

define output filename

```
dataOUT='../data/HCPR3gsr.mat';
```

load parcel label and network spreedsheet

```
AtlasTable = readtable(['../assets/Glasser2016_360Parcels_7Networks.xlsx']);
% AtlasTable = readtable(['./resources/Schaefer2018_400Parcels_7Networks_2mm
Label='Parcel_ID'; % this should be variable name of the numerical label of
System='Network'; % this is the variable name of the numerical label of func
```

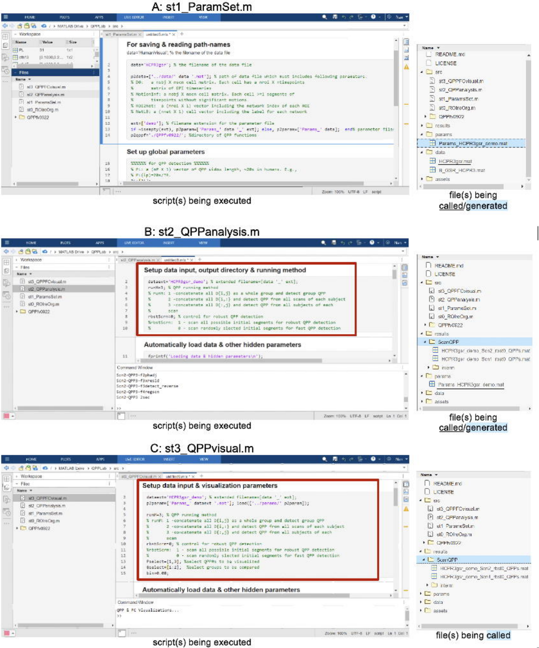
add function files

```
addpath('./QPPfv0922/')
```

Command Window

```
>> load("/MATLAB Drive/QPPLab/data/B_GSR_HCPR3.mat")
>>
```

	A	B	C	D	E	F
1	Parcel_ID	Hem	Area_Nai	Area_Descript	Network	New
2	1	L	V1	Primary Visual C	Visual	No
3	2	L	MST	Medial Superior	Visual	No
4	3	L	V6	Sixth Visual Are	Visual	No
5	4	L	V2	Second Visual A	Visual	No
6	5	L	V3	Third Visual Are	Visual	No
7	6	L	V4	Fourth Visual Ar	Visual	No
8	7	L	V8	Eighth Visual Ar	Visual	No
9	8	L	4	Primary Motor C	Somatom	No
10	9	L	3b	Primary Sensory	Somatom	No
11	10	L	FEF	Frontal Eye Fielc	Dorsal Att	No
12	11	L	PEF	Premotor Eye Fi	Dorsal Att	No
13	12	L	55b	Area 55b	Ventral At	No
14	13	L	V3A	Area V3A	Visual	No
15	14	L	RSC	RetroSplenial Cc	Default	No
16	15	L	POS2	Parieto-Occipita	Frontopar	Yes*



For saving & reading path-names

data='HumanVisual'; % the filename of the data file

```
data='HCPR3gsr'; % the filename of the data file

p2data=['../data/' data '.mat']; % path of data file which must includes following parameters:
% D0:    a nsbj X nscn cell matrix. Each cell has a nroi X ntimepoints
%        matrix of EPI timeseries
% MotionInf: a nsbj X nscn cell matrix. Each cell >=1 segments of
%        timepoints without significant motions
% ROI2Net:  a (nroi X 1) vector including the network index of each ROI
% NetLB: a (nnet X 1) cell vector including the label for each network

ext=['demo']; % filename extension for the parameter file
if ~isempty(ext), p2param=['Params_' data '_' ext]; else, p2param=['Params_' data];  end% parameter file
p2qppf='./QPPfv0922/'; %directory of QPP functions
```

Set up global parameters

```
%%%%%% for QPP detection %%%%%%
% PL: a (nP X 1) vector of QPP widow length, ~20s in humans. E.g.,
% PL(ip)=20s/TR.
```

Setup data input, output directory & running method

```
dataext='HCPR3gsr_demo'; % extended filename=[data '_' ext];
runM=3; % QPP running method
% runM: 1 -concatenate all D{i,j} as a whole group and detect group QPP
%       2 -concatenate all D{i,:} and detect QPP from all scans of each subject
%       3 -concatenate all D{:,j} and detect QPP from all subjects of each
%       scan
rbstScrn=0; % control for robust QPP detection
%rbstScrn:  1 - scan all possible initial segments for robust QPP detection
%           0 - scan randomly slected initial segments for fast QPP detection
```

Automatically load data & other hidden parameters

```
fprintf('Loading data & hidden parameters\n');
```

```
Scn2-QPP3-f2phadj
Scn2-QPP3-f3xresid
Scn2-QPP3-f3detect_reverse
Scn2-QPP3-f4regscn
Scn2-QPP3 2sec

>>
```

Setup data input & visualization parameters

```
dataext='HCPR3gsr_demo'; % extended filename=[data '_' ext];
p2param=['Params_' dataext '.mat']; load(['../params/' p2param]);

runM=3; % QPP running method
% runM: 1 -concatenate all D{i,j} as a whole group and detect group QPP
%       2 -concatenate all D{i,:} and detect QPP from all scans of each subject
%       3 -concatenate all D{:,j} and detect QPP from all subjects of each
%       scan
rbstScrn=0; % control for robust QPP detection
%rbstScrn:  1 - scan all possible initial segments for robust QPP detection
%           0 - scan randomly slected initial segments for fast QPP detection
Pselect=[1,3]; %select QPP#s to be visualized
Gselect=[1:2];  %select groups to be compared
bin=0.08;
```

Automatically load data & other hidden parameters

```
QPP & FC Visualizations...
>>
```

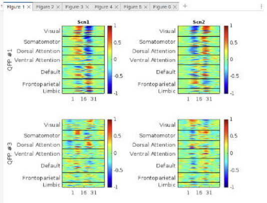


Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
Scn1
Scn2
QPP #1
QPP #3
Visual
Somatomotor
Dorsal Attention
Ventral Attention
Default
Frontoparietal
Limbic
1 16 31
1
0.5
0
-0.5
-1

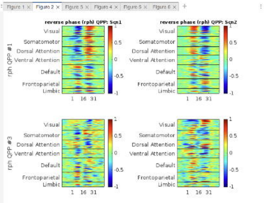


Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
reverse phase (rph) QPP: Scn1
reverse phase (rph) QPP: Scn2
rph QPP #1
rph QPP #3
Visual
Somatomotor
Dorsal Attention
Ventral Attention
Default
Frontoparietal
Limbic
1 16 31
1
0.5
0
-0.5
-1

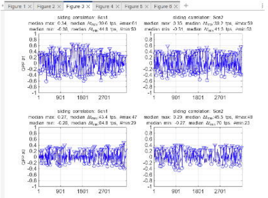


Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
sliding correlation: Scn1
median max: 0.34, median Δt_max:39.6 tps, #max:61
median min: -0.36, median Δt_min:44.8 tps, #min:50
sliding correlation: Scn2
median max: 0.35, median Δt_max:39.2 tps, #max:59
median min: -0.31, median Δt_min:41.3 tps, #min:53
sliding correlation: Scn1
median max: 0.27, median Δt_max:43.4 tps, #max:47
median min: -0.28, median Δt_min:64.8 tps, #min:29
sliding correlation: Scn2
median max: 0.29, median Δt_max:45.5 tps, #max:48
median min: -0.27, median Δt_min:70 tps, #min:23
QPP #1
QPP #3
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1
1 901 1801 2701

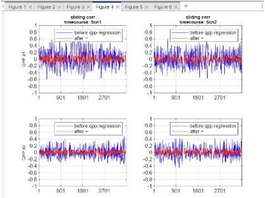


Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
sliding corr timecourse: Scn1
sliding corr timecourse: Scn2
before qpp regression
after ~
QPP #1
QPP #3
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1
1 901 1801 2701

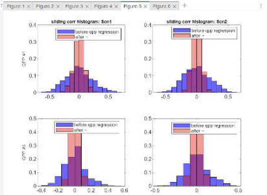


Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
sliding corr histogram: Scn1
sliding corr histogram: Scn2
before qpp regression
after ~
QPP #1
QPP #3
0.4
0.3
0.2
0.1
0
0.5
-0.5 0 0.5
-0.4 -0.2 0 0.2 0.4 0.6

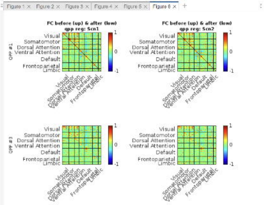
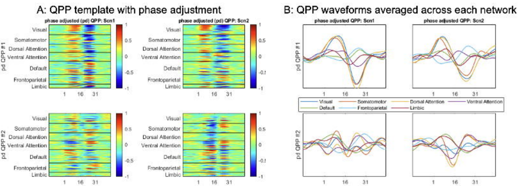
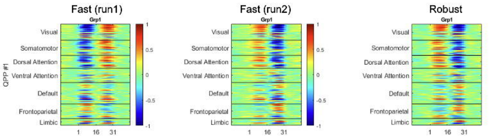


Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
FC before (up) & after (low) qpp reg: Scn1
FC before (up) & after (low) qpp reg: Scn2
QPP #1
QPP #3
Visual
Somatomotor
Dorsal Attention
Ventral Attention
Default
Frontoparietal
Limbic
1
0
-1



A: QPP template with phase adjustment

B: QPP waveforms averaged across each network


Fast (run1)
Fast (run2)
Robust
Grp1
QPP #1
Visual
Somatomotor
Dorsal Attention
Ventral Attention
Default
Frontoparietal
Limbic
1
16
31
1
0.5
0
-0.5
-1