Visualization Techniques of Time-Varying Volumetric functional Neuroimaging Data: A Survey

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Abstract

Within the field of neuroimaging the use of time-varying data is both commonplace and a critical component towards the development of a critical medical diagnosis as well towards the advancement of our understanding of the human brain. Present visual analysis *techniques revolve around two-dimensional (2D) slice representations which though useful in their own right limits access to the spatio-temporal features inherent in these datasets. This work assess the current state of the art with regards to time-varying volume visualizations with a discussion on some of the most common tools used to visualize time-varying medical images as well as providing a discussion on current challenges and techniques when dealing with these complex types of data.*

Categories and Subject Descriptors (according to ACM CCS): I.3.3 [Computer Graphics]: Time-varying—Volumetric Neuroimaging data

1. Introduction

The human brain is an incredibly complex and mysterious organ which has fascinated the human race for ages [BG11]. The study of the human brain shares an equally long and complex history, experiencing constant changes in terms of our understanding of how this incredible structure works [Rai09]. While there are many aspects to the study of the human brain, perhaps the most exciting, or at least relevant within the modern age of Information, is the field of Neuroimaging. Within the study of the human brain, neuroimaging has proven to be an incredibly valuable contributor, both in terms of its ability to elucidate complex cognitive functions within *live* brains, but also as a mean in which to *see* the brain [VHGRG04].

The use of time-varying data within the field of neuroimaging is both commonplace and a critical component towards the development of a critical medical diagnosis for a patient or to one's hypothesis when investigating neural functions such as language processing or visual-cognition [GWL*08, VHGRG04]. Thanks to advances in modern medical imaging, images can be collected faster while still maintaining high spatial resolutions which has opened the door towards the acquisition of larger, more complex multi-modal data [EWS14]. With new technology comes new problems, particularly as data grows in terms of size and complexity [EWS14, VHGRG04]. Present visual *analysis* techniques revolve around two-dimensional (2D) slice representations which, though useful in their own right, can be limiting and often time-consuming when attempting to compare different images of the same patient slice-by-slice, or when attempting to examine changes within a functional network across a collection of datasets, such as those involved in language learning or the progression of neuro-degenerative diseases.

The aim of this work is to provide a survey of visualization tools and techniques used in the representation of Multi-temporal and time-varying volumetric data, with a special emphasis on current and future applications within the domain of neuroimaging. The contributions of this paper include a high level overview of the domain that is neuroimaging as it relates to the types of data used and their role within temporally focused research such as imaging the neural correlates of language learning networks. This paper also offers a discussion of the most common tasks associated with this domain in addition to a high level overview of the State of the art when it comes to visualization methods and techniques currently used by visualization and neuroimaging researchers. Finally, supplementary material has been included from qualitative interviews with domain experts for the readers reference.

2. Domain

Advances in modern medical imaging have paved the way for numerous techniques, such as Magnetic Resonance Imaging (MRI) and Electroencephalography (EEG), which have opened the door towards acquiring complex multi-modal data. One technique, known as functional Magnetic Resonance Imaging (fMRI), has enabled neuroimaging researchers and clinicians to detect metabolic changes within the cerebral tissue. This effect is known as the Blood-Oxygen-Level-Dependent (BOLD) signal and is the result of an increase in oxygen delivery to active cerebral tissue, which in turn results in changes to the local magnetic field. [SRWE07] This provides for high spatial resolution of active brain regions which, when combined with an anatomical reference such as MRI data enables researchers to glean important insights into the complex operations of human cognitive processes, such as learning. However, fMRI data is time-dependent and highly complex, requiring immense preprocessing in order to extract viable signal from the data, and dozen of volumes must be collected in order to capture and model this signal in relation to brain function.

In typical fMRI visualization applications, multiple volumes are rendered individually or in conjunction with one another in an overlaying fashion. This is acceptable if the image(s) in question are static, or represent the averages of multiple sessions. However, studies investigating the progressive degeneration of neural tissue and function, such as corticobasal syndrome and Alzheimer's disease, require several sets of images describing the diseases progression over time. More recently, work has begun to examine how learning networks evolve over time, such as through the course of learning a novel language. In these cases, several series of images are generated which show the progressive evolution of neural networks through time. Through the use of advance statistical analyses and data reduction techniques, additional dimensions become accessible, but which require more advanced visualization techniques in order to effectively represent their meaning and implications. In these cases, existing tools can be cumbersome and limit the user's ability to explore and analyze the dynamic aspects of their data.

It should be mentioned that the terms temporal and time-varying data bear wide interpretations depending on the domain and even the data in question. For the purpose of this survey, when referring to temporal and time-varying in the context of neuroimaging and fMRI data, we mean a temporal *within data* resolution on the order of seconds. That is, a single fMRI data volume typically consists of 100 or more whole brain snapshots. Images are collected sequentially with a latency between 1000ms up to 5000ms. For data collected using systems like EEG, this latency is frequently on the order of nanoseconds. Outside the discussion of fMRI and neuroimaging related data collection methods, the author will provide clarification as needed.

3. Domain Specific Tasks

By the very nature of the data collected, visual tasks are an intrinsic component of the domain's research. A cardinal rule within the domain of neuroimaging, is to *Always inspect your data* ***visually***. This rule lends itself well to visualization in general as proper visual encoding will invariably assist researchers and domain experts towards to the pursuit of understanding their data. The most common tasks include: *Exploration*, *Comparison*, and *Identification*

3.1. Exploration

One of the most important tasks for a neuroimaging researcher is to simply explore data. By visually examining ones dataset, the researcher can gain insight into the structure of the image, its quality, and often some insight into the results. The ability to simply *explore* the data in order to support sense making is a fundamental task in Neuroimaging. Though typically, researchers have a well defined assumption about the contents of their data. For example, a common exploration task involves visually checking for "oddities" and "inconsistencies" potentially residing in the dataset. These "oddities" can be related to subject motion, which is the result of patients moving during a scan, or they could be scanner related artifacts such as a sudden drop in signal in a region of the brain [COA*12]. Dedicated neuroimaging analysis tools, like AFNI [Cox96] and SPM [spm14] have built-in components which enable a user to visually examine their data at each point along the data processing and analysis pipeline. Furthermore, visually assessing the spatial layout of clusters of activation can provide researcher with an accurate sense of the distribution of neural resources the brain employs when solving a task, or, as in the case of disordered brains, where potential sources of problems may be occurring.

3.2. Comparison

Frequently, researchers need to compare one dataset to another, for example when comparing a "typically developing" brain's data to a developmentally impaired brain, or comparing the results of two experimental conditions against one another. Recently, Plante et. al, [PPD*14] explored the neural correlates of novel language learning between a group of controls and experimental subjects. They found that control subjects recruited fewer regions of the brain when asked to listen to 'shallow' stimuli. That is, they were presented with a fake language that for all intents and purpose sounded like natural language, but which had no meaningful information contained within. By contrast, the experimental group showed numerous regions of the brain recruited when presented with real Norwegian sentences. In this instance, simply being able to see on a whole brain scale, the topological differences between the two images can be incredibly valuable towards developing the next steps in a high-level analysis.

Beyond analysis procedures comparison tasks are employed during the preprocessing stages of the analysis as a means of checking that the data is visually conforming to your expectations in terms of those data processing steps.

For example, a common step in processing brain imaging data is to register the 3D grid to a standardized 'atlas' or template space [Rob04]. The underlying principle being that in order to account for the wide variability of individual human brains, 'warping' each individual brain to fit a standardized temple reduces error in inter-subject variability [CJH*12]. It adds further benefit by enabling comparison across studies. That said, alignment algorithms, while certainly robust, are not fool proof and often take many iterations to ensure the supplied image has been correctly aligned. Thus comparison tasks become and intrinsic component of brain imaging from both a high and low level point of view.

3.3. Identification

Identification tasks are yet another critical operation performed by neuroimaging researchers and other experts within the medical imaging community. Given the recent awareness of Traumatic Brain Injury (TBI) within the National Football League (NFL) as well as from soldiers returning home from foreign wars, identifying biological markers indicative of TBI has become an area of significant interest [MRK*14, CVH*14].

It is equally important for experts to be able to confidently identify areas of the brain implicated in a behavioral task, such as identifying the neural substrates of attentive listening. In study by Christensen et. al., [CLAP10], they identified a unique set of neural regions recruited when a participant was asked to identify certain attributes of spoken words. For example, in some cases they were told to ignore the content of the words and only attend to the speaker, while in other instances they were asked to ignore the speaker and focus on the content of the word. Through these tasks they identified distinct neural substrates related to attention and listening.

Finally, it is critical that a doctor or other medical professional be able to quickly and accurately identify neural regions impacted due to Epilepsy or post-operative Temporal Lobotomy [THM*13]. Or when performing preoperative planning for surgeries such as Tumor removal [PSB*11].

4. Survey

There has been a growing trend over the past 10 years of so within the field of scientific visualization towards generating and interacting with large time-varying volumetric datasets and the domain of neuroimaging is no exception. However, understanding and exploring these datasets is still a major challenge both in terms of managing and expressing the dimensionality of many of these types of datasets as well as dealing with their size [ZEP12, KH13]. Furthermore, rendering this kind of data in real time requires the use of some form of compressed representation as it is not feasible to interactively render every time step in the GPU in real time [BRGIG*14]. Though numerous techniques have been developed to address these issues, often they are limited to the specific question they were designed to address [AMM*07] and differ widely depending on their treatment with regards to the temporal dimension [WOM13]. With that in mind, advances in hardware acceleration and programmable GPU's have made it easier to develop high-resolution multi-volume rendering, and numerous applications have been developed to take advantage of this. The remained of this survey will spend time examining visualization techniques and applications employed by non-medical scientific fields and their approaches to the challenges highlighted herein. These techniques include the use of particle-based rendering methods in place of more traditional volume rendering techniques and surface-based mappings. Finally, a discussion on multiple linked views and their applications towards the use of visualizing time-varying volumetric neuroimaging data will conclude the survey.

4.1. Particle-Based Rendering

Within the medical imaging domain, volume rendering techniques are a popular means of representing ones data [VSSK12]. The need for fast, interactive visualization techniques are in high demand and while many such techniques exist [KH13], often they are incapable of scaling to handle time-varying datasets [ZSK14]. Recently, work has been done exploring the use of particles-based rendering (PBR) methods to circumvent some of the more common hangups, such as low frame-rates and the need for object sorting which can be computationally expensive. For example, particle-based methods typically do not require depth sorting. Furthermore, graphics hardware being what it is today, PBR greatly benefits from their parallelized design [VSSK12, ZSK14]. One application for this technique involves the fusion of different types of objects represented in a medically based visualization. For example, being able to display both the structural gray matter based brain images fused with fMRI brain images provides a clear representation of the topological layout of neural activity. A non-PBR technique was demonstrated in a paper by Forbes et. al., [FVAP14]. In their work they present a prototype application which used a naive Isosurface Raycasting technique to displayed multiple fMRI activation meshes fused together with a structural brain mesh, resulting in an interesting visualization of functional brain/language networks evolution over time. That said, the application suffers performance wise due to the large number of volumes used. Though their technique is somewhat naive, it does illustrate the limitations, particularly when it comes to volume rendering, when trying to show multiple datasets at the same time. Often this is not feasible, at least at interactive frame rates, as the underlying datasets can be quite large. This is especially true when dealing with time-varying datasets.

To address that problem, Zhao et. al., [ZSK14] developed

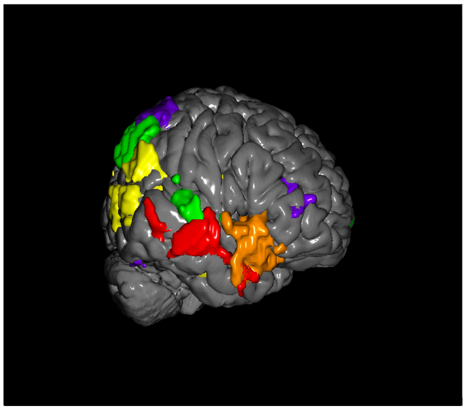
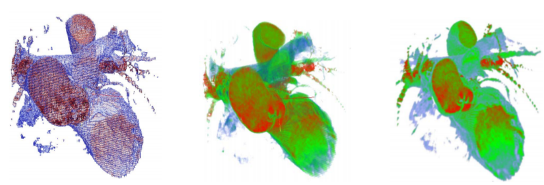


Figure 1: *3D+Time Brain View [FVAP14] Using an Iso-surface raycasting technique to render in detail a functional language network*

a particle-based rendering technique that is capable of handling large volume datasets and can easily fuse multiple objects together through the use of proxy geometries. Furthermore, their method allows researchers to not only render their data at interactive frame rates, but also allows for easy switching between datasets by performing an initial Raycast which determines the bounds and overall shape of the image. They circumvent the need for object sorting by redefining the nature of object opacity. Usually, opacity is determined from a Transfer function, however Zhao et. al., use a density function of emissive particles. Thus they mimic the effect of opacity by substituting it with density of points.



(a) Wire-frame surface, $\frac{1}{2}$ mesh-resolution (> 30fps)

(b) Projected tetrahedrons, volumetric (< 0.1fps)

(c) PBVR, volumetric (16.4fps)

Figure 2: *Adaptive Particle-Based Rendering system showing the different frame rates available depending on the visualization type. Notice the middles image, which uses traditional mesh based visualization has a painfully slow frame rate, while the APBR system show acceptable levels while also maintaining the same quality of the representation*

4.1.1. Surface Mapping

A popular technique, especially among neuroimagers is the use of surface based visualizations via volumetric meshes. Surface-based neuroimaging analysis is advantageous for at least four reason:

1) It maintains the topology of cortical gray matter activation. Due in part to the sampling size and resolution of the volume itself, neighboring voxels within the brain are not necessarily sampling neighboring cortical structures. This is in part due to preprocessing techniques in which voxel data is smoothed resulting in the loss of topological information. By mapping the activation data from the volume to the surface domain, data processing measures can be conducted on the surface itself, resulting in *improved* topological detail.
2) Surface-based analyses increase statistical power [ADG*08] due in part to the improved topology and coherence between voxel information and surface mesh nodes.
3) Cortical thickness is easy to calculate through the use of an inner and outer gray matter meshes.
4) Very high quality visualizations of structural and functional brain data [SR12]. While all of these benefits can be accomplished using volume-based approaches, the computational complexity is much higher. The only overhead that is typically encountered is in the initial creation of the surface mesh, which has been alleviated somewhat with the latest advances in hardware support and more effective registration algorithms and software.

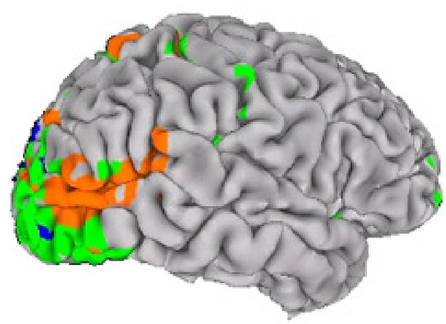


Figure 3: *SUMA [SR12] A pial gray matter mesh with mapped voxel information*

Several applications have been developed for the purpose of surface based analysis of neuroimaging data, including FreeSurfer [Fis12], Caret [VEDD*01], and SUMA [SR12], from the creators of a very popular neuroimaging statistical analysis package called AFNI [Cox96, Cox12] (described in more detail below). Assuming a representative surface mesh is available, it is easy to link the 3D surface mesh to the 3D volume data, allowing for one to interact with their data in several dimensional views. Furthermore, all renderings are connected such that clicking on any surface, whether 2D or 3D volume views, updates the crosshair location on all visualizations, including time-series graphs. A more recent application

4.2. Multi-linked Views

The concept of multiple linked views can trace its origins to that of the InfoVis and has been a popular technique when displaying multi-modal and multi-temporal data for the past 20 years [KH13]. The use of multiple views is advantageous in that it allows the user to explore different data variables and attributes side-by-side employing well known visualizations into a single interface.

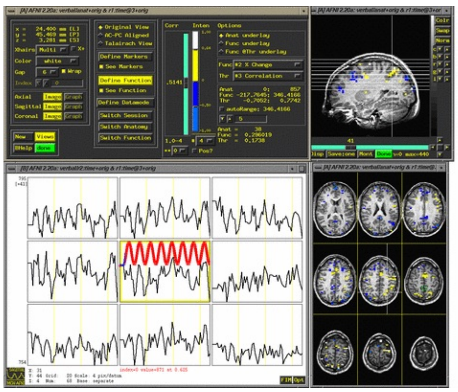


Figure 4: *AFNI [Cox96, Cox12] 2D orthogonal layout with a linked time-series graph view of the selected variables, in this instance 16 voxels across 164 time points*

Presently there is a wide range of popular tools which neuroimagers employ to not only process and analyze their data, but also to visualize it as well. The most popular tools used by domain experts within the field include including FSL [SJW*04, WJP*09] and SPM [spm14] AFNI [Cox96, Cox12]. AFNI is a UNIX-based open source software package for the Analysis of Functional Neuroimaging data. AFNI follows the guided principle that as a tool it should allow a user to stay close to their data with the ability to view it in several *different* ways. In this way a user is able to become familiar with the structure and results of their data. AFNI offers good support for both 2D, 3D, and 4D data representations by taking advantage of representational views the datasets dimensions. For 4D data, it visualizes temporal information as an interactive time-series graph which, when specific points are selected, updates the 2D orthogonal view of the data to show that point in time. They have also integrated a feature in which the selection mode automatically traverses the time-series graph, updating the 2D view in kind. This can be useful when examining a dataset for subtle changes within the signal as well as when tracking artifacts due to motion, for example.

Li et. al., [LGF*12], discusses a novel visual analytics approach in which integrate multimodal neuroimaging information into a unified framework via joint modeling of said multi-modal data, as well as data visualization and intuitive user interface. The paper primarily focuses on the application and its features, though it provides a comprehensive

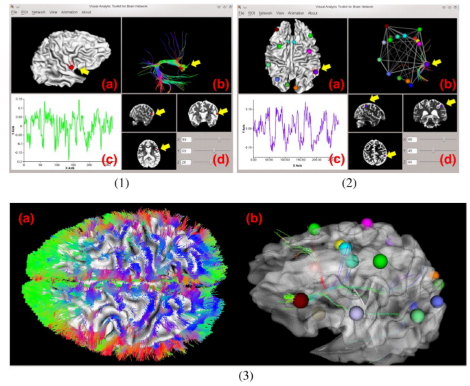


Figure 5: *VAST [LGF* 12] Showing two sets of linked views of multiple representations of connectivity data, including structural connectivity data, evidenced by the Diffusion tensor images (DTI), functional connectivity data as evidenced by the time series graph, and a volume rendered brain*

analysis of the HCI component. The tool incorporates every type of neuroimaging data, from DTI, functional ROI maps, and structural anatomical images and encourages the inclusion of all modalities for maximum effectiveness. Though able to offer numerous image processing functionalities, this system is through and through a network visualization system with the various modalities supporting the application in that task. Additional features include a network prediction algorithm which attempts to localize single subject ROIs in relation to group activation networks.

5. Future Directions

Present visualization techniques for for time-varying volumetric visualizations of neuroimaging data have been well established within their respective community. However, as data continues to grow in complexity, and data collection hardware improves in terms of its resolution, more advanced techniques will need to be employed. The use of Particle-based rendering methods presented earlier may have some involvement in this future as they offer better performance for similar encoding of the same data. In nearly every case the use of multiple-linked views will likely dominate the development of these tools as so far there does not seem to be a one-view-fits-all model, and arguably there shouldn't be.

6. Conclusions

Based on the provided survey of the state-or-the-art of Multi-temporal volume visualization of functional neuroimaging as well as the responses from Domain experts, it is clear that each representation of time-varying data is valuable in its own right. However, no single visualization is capable of meeting every need of the user, nor should it. Instead, a best of both worlds approach should be pursued by marrying some or all of these techniques into coordinated multiple views which take advantage of well-known visualizations such as appears to be the most desirable in terms of the needs outlined by the domain experts.

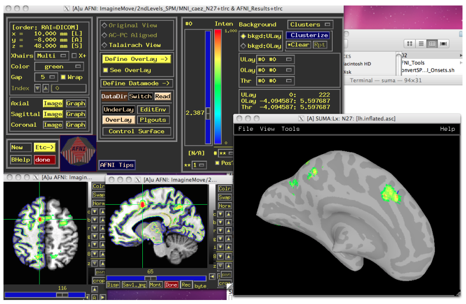


Figure 6: *AFNI and SUMA with linked functional data showing how multiple representations improves visual analysis and exploration of the data in question*

7. Domain Perspectives

The following section examines domain expert's perspectives on current visual analytic tasks within the domain of neuroimaging

What is the main research project you work on?
Expert 1: Imaging the neural correlates of language learning by typical adults and adults with developmental language impairments. This primarily involves functional MRI data, but we also collect diffusion tensor images that are used to visualize white matter pathways.
Expert 2: Neuroimaging correlates of recovery from aphasia after stroke

What would be an ideal result from your research?
Expert 1:We identify the brain regions that are instrumental to learning and how people recruit these neural resources during the learning process. We then identify which subsystems are not used optimally when learning is impaired , either because regional resources are not recruited enough, or because they are recruited at the wrong time.
Expert 2: To show that certain patterns of reorganization are associated with recovery of language function, whereas other patterns are associated with persistent deficits.

What kind of data do you work with most often in your research?
Expert 1: MRI imaging data. The data are dicom images that get converted to other formats (e.g., nifty format) and are processed in multiple ways to produce analyzable data. FMRI data is 4-D data. DTI data is 3D data.
Expert 2: In descending order, fMRI, behavioral measures of language function, structural MRI, DTI, ASL perfusion.

How do you gather or generate this data?
Expert 2: MRI scanner, record and analyze interactions with patients

How is this data used/analyzed?
Expert 1: There are two basic steps for all imaging analysis. **1)** preprocessing that converts native data into other formats, removes signal variation that are not of interest and/or are confounding (e.g., movement, alignment, spikes, slow drift). **2)** statistical analyses of the preprocessed data. For functional imaging, this involves statistical procedures designed to detect signal variation associated with task performance and possibly additional statistics that look for associations with behavioral performance metrics, group differences, and other conditions.
Expert 2: Changes in neuroimaging measures over time are correlated to changes in language measures.

What visualization tools/techniques do you use to help make sense of this data?
Expert 1: The primary tools we use are visualization components available in AFNI, FSL, SPM software programs. These are all freely available and include analysis software and limited visualization tools. We also use Almryde's nifti viewer
Expert 2: AFNI, MRIcron, MATLAB (custom scripts)

What visualization tools/techniques do you use to display the data and/or communicate with other experts in your field?
Expert 1: Publications still use 2-D images primarily. However, journals are now offering 3-D on-line viewers that authors can upload their data into. No one offers a 4-D viewer yet.
Expert 2: Exactly the same.

What type of visualization tools / techniques would you like to see which could help you make better sense of your data
Expert 1: I would like to be able to marry data obtained from different imaging techniques (e.g., structural MRI, fMRI, DTI tractography) into one 4-D viewer. I would also like to link other statistical data (e.g., magnitude data) and graphic displays (e.g., bar or line graphs) with the underlying data within a brain region.
Expert 2: I wish there was a tool that combined the best features of AFNI and MRIcron. i.e. the way AFNI handles 4D data is very nice (showing plots of time series for each voxel, etc.), whereas MRIcron excels in overlaying multiple functional images, and in 3D surface renderings.
I also wish that my image viewing tool would generate

publication-quality images without having to use photoshop/illustrator to put figures together.
I wish I could save a "view" which would be a set of images/overlays/etc, to come back to later.
It would be nice to have better tools for model diagnostics, i.e. seeing how well the GLM fit the data in different voxels.
I wish it were easier to combine data from multiple modalities, i.e. easily turn layers on and off, derive RGB values from images of multiple types, etc.

Do you find Direct Volume Rendering visualizations of the brain (Such as the NifitViewer) are useful, or are they just another pretty picture?
Expert 1: This can go either way. For many very basic studies that use simple analyses and study one fairly static phenomenon, I think it is probably just a pretty picture for those of us who really have a strong internal reference for the 3-D brain. I think as we begin to exploit the time parameter more in fMRI research (this is coming), this will become more important because it is hard to get your mind around both regional and timing changes at the same time without a viewer.
Expert 2: Surface renderings as in MRIcron are a very useful way of getting overviews of patterns, and sometimes of presenting those patterns in a straightforward way in publications.

Do you employ any tools which allow you to visualize temporal changes in the brain? If so, what are they and what about them do you find useful?
Expert 2: AFNI for raw temporal changes. Any functional image is derived from temporal changes of course. AFNI is good for temporal changes because it lets you plot the timecourse of any voxel, or small region of voxels, etc.

How do you feel about neuro-imaging tools being deployed online rather than locally like a traditional application? Assuming the application and work with your data locally, rather than making you upload it to some strange server, etc, do you feel there would be an advantage to having web based neuro-imaging tools/visual-analytic tools?
Expert 2: For most tasks, I think the best setup is a local system in which updates are deployed seamlessly, i.e. debian/ubuntu. I don't really understand what software deployed online would gain you if the data is local anyway. I can see some situations in which very computationally intensive analyses could be performed in a cluster by some online tool, but that would require uploading your data.

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