**IMaGES iFAQ (inFrequently Asked Questions)**

1. What is IMaGES?

IMaGES is a module which is inside of a more general modeling tool (like SPSS, Matlab or R) called “Tetrad”. It stands for Independent Multisample Greedy Equivalence Search. It is a program used for effective connectivity ("causality") analysis of fMRI data.

Tetrad was developed by Clark Glymour and colleagues at Carnegie Mellon; IMaGES is actively codeveloped by Steve Hanson (Rutgers), Russ Poldrack (UT Austin) and Joe Ramsey (CMU). This project is funded by the McDonnell Foundation.

We pronounce it “Ee­maah­jes” kind of like calling Target “Tar­jay.”

2. What does IMaGES do?

Fancy smart things, or in facebook terms: it’s complicated. Some of the description below will likely sound like gobbledygook so I’ve provided some references afterwards that help orient those new to graph theory.

IMaGES operates on the assumption that causes precede effects temporally. An illustrative example of this concept is that “a wet sidewalk doesn’t cause rain; rain causes a wet sidewalk.” The algorithm starts with an empty graph and searches forward, one new connection at a time, until it finds the connection that optimally represents the entire group of subjects, interpolating any missing data. It does so with the restriction of finding only Markov equivalence classes of directed acyclic graphs. The process is penalized to prevent overfitting using the Bayes Information Criterion (Schwarz, 1978): \(-2\ln(ML) + k \ln(n)\), where ML is the maximum likelihood estimate, \(k\) is the dimension of the model ( the number of directed edges plus the number of variables), and \(n\) is the sample size.

To understand what IMaGES is doing, it is helpful to become acquainted with the basics of graph theory. Recommended reading for the novice includes this short 5-page overview of causal inference from graph modeling:


Direct link: [http://tuvalu.santafe.edu/~cmg/compmech/tutorials/cstgcm.pdf](http://tuvalu.santafe.edu/~cmg/compmech/tutorials/cstgcm.pdf)

For those already acquainted with directed acyclic graphs, Markov equivalence classes and such, here is the citation for the methods paper for images:

If none of the “six problems” paper makes sense to you, it is recommended you go back and read the first paper. If all of that made sense to you, then go ahead and read the second methods paper which includes an additional module, LOFS, as well as a further simulation study:


3. I am not going to actually go read all that stuff. What is a Markov Equivalence class? How about a directed acyclic graph?

This answer is paraphrased loosely from Clark Glymour’s book “The Mind’s Arrows: Bayes Nets and Graphical Causal Models in Psychology.” If you like this answer, you should go buy the book: http://www.amazon.com/The-Minds-Arrows-Graphical-Psychology/dp/0262072203, No, Clark did not pay me for this endorsement. And yes, much of this explanation is oversimplified for the sake of not making you throw your hands in the air.

Imagine you are a small child playing with a toy train that has three cars all attached to each other - the head car (A), the middle car (B), and the caboose (C). Your first impulse might be to grab the front car. If you were to do so, you would of course notice that pulling the front car A also pulls the second car B. This is a causal relation - pulling A causes B to move, every time, even if it just means that B shifts a little bit. However, sometimes if you pull hard enough, C will start to move as well. However, for C to move, B has to move first. You couldn’t somehow pull car A and manage to only move A and C (unless you were a wizard, which you are not, at least in this example. This is a FAQ, not Harry Potter). Thus, C’s movement is independent of A’s, conditional on B. This describes a conditional independence between A and C, and thus the train meets the criteria for a Markov Equivalence class. A Markov class is simply a restriction placed on directed acyclic graphs because it makes sense theoretically for a variety of reasons, mainly that the method aims to recover essential graphs, or the best most awesome graphs ever that don’t overlap with other, less awesome graphs. We don’t want our graphs fighting over paternity on Jerry Springer, after all.

This toy train system is also a directed acyclic graph because the caboose does not loop back and connect to the head car. Creating a “closed circuit” like that would make it a cyclic system. An acyclic system is one in which the initial input has no other inputs to itself. This is mostly for simplicity’s sake, because allowing cycles into the graph exponentially increases graph space
and the number of calculations that must be done. However, in recognition that the brain may indeed have cyclic graphs, a program to retrieve these structures from brain data is Coming Soon.

3.5. Can’t you just draw me a picture or something?

Ok fine. Here’s a picture. This is the IMaGEs work flow, conceptually.
4. Ok but what do these circles and lines mean? What is it doing with my fMRI data?

Circles are nodes (in fMRI, your regions of interest) and arrows are edges. The direction of the arrow indicates the chain of influence, i.e. A -> B means activation in A is predictive of subsequent activation in B.

5. Isn't this the same as methods like seed correlations, dynamic causal modeling, structural equation modeling, and granger causality?

No - those methods measure functional connectivity, or attempt to measure effective connectivity but have notable limitations such as having to prescribe a model in advance, as with SEM, or the method not being developed with BOLD data in mind, as with granger causality. In fact, there is a growing appreciation that Granger causality may not be appropriate for fMRI time-series (e.g., Nalatore et al, 2007) and performs poorly in comparison to structural (non-dynamic) approaches based upon partial correlations (Smith et al., 2010).
IMaGES improves upon these methods in that it was designed specifically for use with neuroimaging data. It searches over a much less constrained set of graph structures for effective connections in the areas selected using a feed forward approach. Thus, a model does not need to be prescribed in advance, and a much larger model space is searched, yielding higher accuracy in identifying actual causing connections - 90% precision has been reported in the recent simulation study (Ramsey, Hanson, & Glymour, 2011).

IMaGES also capitalizes on the information provided by multiple subjects in order to determine graph structure. This includes a feature that allows interpolation of time points more discrete than the time to repetition (TR) used for the original fMRI data collection, shifting the lag of each time series by 0, 1, and 2 to capture varying hemodynamic response times in different areas of the brain.

Here is a nice schematic from the simulation paper summarizing the effectiveness of IMaGES over other comparable methods - note IMaGES was compared to ~30 other methods and outperformed them all, while other methods were doing near chance on the Smith et al 2010, benchmarks:

**IMaGES Wins!**

Orientation Precision

![Graph showing precision and recall for different methods](image)

**PRECISION: 98%  
RECALL: 90%**

6. How do I use it?
If you are using FSL (FMRIB’s Software Library) and running Ubuntu, you can use the processing stream we use exactly how we use it. If you’re using AFNI, my condolences. You can probably still use these instructions, translated into AFNI-ese (or AFNEESE; bless you). Other packages such as Brain Voyager, SPM, etc. should also conceivably have time series extraction tools.

1. Register your data into standard space using FLIRT.
1.5. Since FSL flattens registered data into a single volume you will need to use the following command line option to recreate a 4D dataset and put the “time” back into your data. The example_func2standard.mat would be output from the registration you ran in step 1. You should run this from the command line while in the registration directory of your data to make things easy on yourself (or you could script this in BASH or python if you have a lot of subjects, but it runs in a few seconds, so it’s up to you).

   flirt -in YourOriginalBOLDdata -ref YourAtlas -applyxfm -init example_func2standard.mat -out Your4DVolume

2. Create masks for your regions of interest using the atlas of your choosing - the Harvard-Oxford is recommended as it is probabilistic and has specificity that is a nice intermediate between the Tailarach (very specific) and MNI (very broad).
3. Extract timeseries from ROIs using FSL’s meanTS module. You can extract an average over the whole ROI, or extract all the time series for every voxel in the ROI and then run a PCA on them (or not), or whatever you’d like really.
4. Assemble the time courses of interest into a matrix per subject saved in a text file format and input these into IMaGES; now you are ready to go.

The equivalent AFNI functions seem to be the following:

Some sort of time series extraction tool -seems similar to fsl MeanTS, but it extracts a "principle singular vector" - of course it doesn't tell you if that means it's actually running a PCA or not. They spend more time making fun of BASH they telling you what it is doing statistically.

http://afni.nimh.nih.gov/pub/dist/doc/program_help/3dmaskSVD.html

Voxel time series extractor thingamabobble:

http://afni.nimh.nih.gov/afni/doc/faq/75

Once your data is in IMaGES you should follow the workflow outlined here:

7. What about other preprocessing steps, like motion correction, high pass filtering, etc?

IMaGES is like the honey badger in this respect in that it just doesn't care.
It is important to note that IMaGEs is using residuals from an autoregression procedure to interpolate timepoints more discrete than the TR. Counter to the conventional thinking about fMRI, noise is actually beneficial to this approach, in that the variance in a non-Gaussian distribution is what allows the data to be predictive (similar conceptually to how ICA works, if you're familiar).

To this end, "useful noise" is good and "useless noise" or Gaussian data just gets discarded or ignored. A spike in motion leading to a fake spike in activation would not be predictive, and would not be included in the model. In extreme cases (i.e. where motion would displace TRs so much that you might not be extracting the right ROI from your BOLD data) it may be prudent to use a motion correction module such as MCFLIRT.

Generally speaking, removing random TRs corresponding to motion would be neutral or even beneficial to the model because it would add noise. Removing a block of stimuli related TRs would be non-random, and would be bad because it would take away predictive information from the model.

So basically: some amount of motion-related artifact is fine, removing a few TRs associated with motion here and there is fine, interpolated TRs are fine, everything is gravy with IMaGEs.

8. Thank you! You have answered all my questions, both about IMaGEs and life in general with your helpful document. If for some strange reason I become confused in the future, can I contact you with any further questions?

Yes, we are happy to answer questions. My email is cfinnerty@psychology.rutgers.edu.