Purpose

- My very first paying project as a consultant was developing tools for analysis of blood flow in the retina with Dr Robert Flower from John Hopkins.
- Understanding Retinal blood flow is critical in diagnosing and treating Age Related Macular Degeneration (AMD) and other disorders.
From 1995 - 2007 we used Indocyanine Green (ICG) angiography to watch “blood” flow through the retina.

- Since ICG mixes with the blood plasma we really aren't seeing what the Red Blood Cell's (RBC's) are doing.

VIDEO
Purpose (cont)

- In 1999 Dr. Flower developed a method for forcing ICG into individual RBC's.
  - Original sequences were taken with a slow and low resolution 8bit video and did not appear to be of much interest
  - In 2007 a 30 fps, 12 bit low noise camera was used to gather new sequences and the results were astounding
  - Now it is possible to watch individual RBC's as they move through the retinal blood vessels - VIDEO

- Opens up a brand new set of questions to answer.
  - Do RBC's travel with a constant velocity?
  - If not, what does it look like?
Purpose (cont)

- Unfortunately, new problems also arise.
  - Registration is more of an issue since we want to accurately track each RBC
  - The physiology of the eye causes a background “noise” to be present
- The rest of the brief shows the process we go through to massage and analyze the data
- All of these algorithms I was able to get from other people or on the web
Surprising results

- When we watch the video three things are obvious
  - There is a strong background component made up of fuzzy RBCs, these are behind the retina
  - There are two populations of RBCs on the retina
    - The largest group are constantly moving
    - The second group stop and start
- We are in the process of studying this stopped group and don't have any definitive explanation as to why they stop
- Accurate tracking requires that the images must be accurately registered. Otherwise we won't know if particle movement occurs from a velocity or the eye moving
Problem #1 Registration

- There are literally dozens of automatic image registration algorithms
  - Most are slow
- In 2003 Xonjie et al published an IDL algorithm for ENVI that uses an FFT technique
  - Ideal for images with sharp edges like lines or well defined points.
  - Is a global method, gives translation, rotation and scale for entire image. i.e. it does not do warping
  - FAST – VIDEO
Registration

- Start with an image of a triangle then shift it by 50 pixels in x and y for the second image.
Registration

- Real part of FFT's are nearly identical, but the phase images are different.
- Technique involves taking the complex conjugate of the two images (basically a division) and result will give a single peak at the optimal alignment!
Restrictions on this method

- Images must share common features. Trying to align a Landsat image with a radar image probably won't work.
- Images must be the same size.
- If you also need to do rotation and scaling the images have to be square.
- Overlapping area has to be at least 30%.
- Scale change between images has to be less than 1.8.
- Will not work if there are non-linear distortions.
In 1996 Crocker and Grier published the definitive paper on particle tracking over small scales.

- They did all of this in IDL and make their code publicly available for download (http://www.physics.emory.edu/~weeks/idl/)

They break tracking into two parts

- First you must isolate the particles from the background. This is done with a combination of band pass filtering, edge enhancement and smoothing
- Second a network flow technique is used to track identified particles from one frame to the next.
Enhancing the stopped RBC's

- We have two challenges with analyzing the stopped RBC's
  - In the raw images the stopped RBC's fade in and out
  - The presence of so many moving RBC's make identifying the stopped ones much harder
- What we want to do is apply some type of a filter to make twinkling RBC's constant and the the fast moving RBCs disappear
- The way to solve this problem is to look at a single pixel over the full sequence
Reality vs Desired

- Top curve is a profile of what a stopped RBC intensity over time might look like.
- The profile that I want is the bottom curve. Variations have been evened out, but not in a smoothing kind of way.
- Classic analysis would use an FFT to pull out the dominant signals.
When not to use an FFT for analysis

- FFT's are designed for systems that are linear and strictly periodic or stationary. If they are not then the decomposition will not have *physical* significance.
  - The emphasis on physical is important. We can accurately decompose any signal via FFT, but do the components have a physical reality. They will, but only for the conditions above and that is critical.

- Consider trying to use a series of sines and cosines to model a flash of light.
Light Flash

- The flash is very localized in time
- In order to compensate the FFT has to generate many frequencies both positive and negative so that they add up to make the spike
- So what is a negative frequency of light?
Hilbert Huang Transform

- It was this paradox of using FFT's on real data giving non-real decompositions that led Huang et al. (The empirical mode decomposition and the Hilbert spectrum for nonlinear and non-stationary time series analysis, 1998) to develop a data-driven technique that will work for real data.

- It is simple, elegant, and I am really mad that I didn't think of it.
  - Gives me hope that there a still great algorithms out there waiting to be discovered!
HHT

- The idea is to find a set of characteristic points that define the curve and fit a spline through them. This spline has to fulfill two conditions.
  - In the whole data set, the number of extrema and the number of zero crossings must either equal or differ at most by one
  - At any point, the mean value of the envelope defined by the local maxima and the envelope defined by the local minima is zero.

- Huang developed a simple iterative process called sifting that creates the splines that he called Intrinsic Mode Functions or IMFs

- Daithi Stone (http://www.csag.uct.ac.za/~daithi/) developed a set of IDL routines for processing data with HHT.
HHT on the Pixel Intensity Data

- Original data on top
- First IMF on bottom
- Number of extrema is 12, number of zero crossings is 12
- Notice how the bottom plot looks like a wave that is riding on the data in the top plot
HHT (cont)

- This IMF is then subtracted from the original data to give the first residual and this gives the exact profile that we want.
- In the classic HHT this process is repeated until the residual is a monotonic function.
Conclusion

- I fell in love with IDL almost twenty years ago and I still feel the same way.
- The key to keeping IDL as the desired tool is to incorporate new algorithms as quickly as possible so that we can all use them in our research.
- Questions?