Overview

• Optical Coherence Tomography (OCT)
  – Brief History
  – Overview of the Modality
• Methods and Applications in Ophthalmology
  – Image pre-processing
  – Layer Segmentation
    • Graph-based
      – 1d
      – Graph Cuts
    • Shape-based
  – Optic Nerve Segmentation
  – Image Registration
• Other application domains of OCT
• Future trends
OPTICAL COHERENCE TOMOGRAPHY

The 6th Imaging Modality

http://www.lantislaser.com/home.asp
OCT in a Nutshell

- OCT:
  - Based on light back-reflected from within a medium
  - Optical analogue of Ultra-Sound
  - Is Non-Invasive and contactless
  - Is an Interferometric technique
  - Generates high-resolution, cross-sectional images
  - Applicable to semi-transparent materials

Optical Coherence Tomography

- At the detector we have a signal only when $z_{\text{ref}} = z_{\text{eye}}$
- This is known as coherence gating
- The axial resolution is limited by the bandwidth of the light source

It can be shown that the measured spectrum of the interferometer output contains the same information as an axial scan of the reference arm. The map of optical reflectivity versus depth is obtained from the interferometer output spectrum via a Fourier Transform.

Applications

- **Biomedical Examples:**
  - Ophthalmology
  - Endoscopy
  - Dermatology
  - Dentistry
  - Microscopy

- **Material Sciences Examples:**
  - Any layered structure of interest
    - Multilayered foils, foods, paintings and artwork, printed electronic circuits, etc

Huang et al. Science, 1991

A Comparison of Optic Nerve Head Morphology Viewed by Spectral Domain Optical Coherence Tomography and by Serial Histology
Strouthidis et al. IOVS, March 2010, Vol. 51, No. 3
OPHTHALMOLOGY AND OPTICAL COHERENCE TOMOGRAPHY

Eye Anatomy 101

Fig. 1.1. A drawing of a section through the human eye with a schematic enlargement of the retina.
Leading causes of blindness in the US

About 1.75 million U.S. residents currently have advanced age-related macular degeneration (AMD) with associated vision loss, with that number expected to grow to almost 3 million by 2020.

Approximately 2.5 million Americans estimated to have Glaucoma.

40 to 45 percent of Americans diagnosed with diabetes have some stage of diabetic retinopathy. That’s ~10 million people. It can lead to blindness.
Ophthalmology

- The patient positions their chin on a chin rest
- The operator acquires the image once the scan patterned is positioned
- The image is captured based on the back scattered light

Analysis Algorithms

- Are fundamental in the use of the instrument
- Minimal requirements are:
  - Layer segmentation
  - Image Registration
  - Motion Correction
IMAGE PROCESSING IN OPHTHALMIC OCT

What software is available

• Commercial
  – Matlab
    • Special purpose toolboxes
    • Academic source code
  – Intel Performance Primitives (IPP)

• Open Source
  – VL feat
  – Open CV
  – ImageJ
  – Generic Image Library
  – Insight Tool Kit
Retinal Layer Segmentation

• Total Retinal Thickness is perhaps the most fundamental analysis method in ophthalmic OCT images

• Fortunately, this measurements is based on the two most obvious layers; the ILM and the RPE:


Dry Age-Related Macular Degeneration

Giovanni Gregori, Ph.D., of Bascom Palmer Eye Institute - [http://www.ophmanagement.com](http://www.ophmanagement.com)


IMAGE PRE-PROCESSING

Noise reduction
Speckle Noise

• Due to constructive and destructive interference
• Reduces contrast and makes boundaries between highly scattering structures difficult to resolve
• Approximately follows a Rayleigh distribution

Schmitt et al., SPECKLE IN OPTICAL COHERENCE TOMOGRAPHY, JOURNAL OF BIOMEDICAL OPTICS 4(1), 95–105 (JANUARY 1999)

Speckle Noise Reduction

• Median Filter
• Sticks algorithm
  – Directional Filtering
• Anisotropic Diffusion Filtering
  – Edge Preserving Smoothing
    • Yu and Acton, Speckle Reducing Anisotropic Diffusion, IEEE TRANSACTIONS ON IMAGE PROCESSING, VOL. 11, NO. 11, NOVEMBER 2002
Median Filtering

Data courtesy of Robert Chang MD, Stanford School of Medicine

Ishikawa et al.


Uses median filter and A-scan alignment
Sticks Algorithm

http://www.mathworks.com/matlabcentral/fileexchange/14862-sticks-filter/content/sf.m

Data courtesy of Robert Chang MD, Stanford School of Medicine

Pre-Processing & Down-sampling

Data courtesy of Robert Chang MD, Stanford School of Medicine

Hu et al.
Two key approaches are coming to the fore

**INTRA-RETINAL LAYER SEGMENTATION**

More Recent Developments in Image Processing

- **Graph-based methods:**
  - Mathematical advances in the field of graph theory has led to optimization techniques applicable to N-D graphs (or images)

- **Statistical shape models:**
  - Techniques to represent prior knowledge of an object of interest’s shape/appearance
    - Constrains optimization space
    - Fills in noisy data
1d Graph Traversal

GRAPH-BASED

Images cast as Graphs

Graph \( G=(V,E) \)
Dijkstra’s Algorithm

1. Set source node as current node, set to 0, set all others to infinity. Mark all nodes as unvisited.

2. For each unvisited node adjacent to the current node, do:
   - If the value of the current node + edge is less than the value of the adjacent node, change the value to this value.
3. Set current node to visited. If there are still some unvisited nodes, set that with the smallest value to the current node, and go to 2. Else, finish.

http://www.algolist.com/Dijkstras_algorithm

Dynamic Programing

Seattle $200
San Jose $180
San Diego $350

Duluth $180
St Louis $170
Dallas $150

Boston $240
New York $300
Miami $220

i=0..2
j=0..2
Create Minimum Cumulative Costs

Dynamic Programing
Create Minimum Cumulative Costs

Cheapest traversal from east coast to west coast?

San Jose $180 → Duluth $530 → Boston $900

San Diego $250 → St Louis $170 → New York $300

Additional weighting can be added to penalize the traversal if it deviates from a straight line.
Typically, this is done by adding a smoothing term, \( h(l) \), with associated costs:
- Where \( C \) is our cumulative cost image, and \( c \) our cost image:
  \[
  C(i+1,j) = \min_{-m \leq l \leq m} C(i,j+l) + c(i,j+1) + h(l)
  \]
- This actually allows us to change the bias “on the fly” pushing the segmentation path upwards or downwards as conditions indicate.

The Smoothing Term

- The smoothing term, \( h(l) \), affords you a lot of control over the path taken
- This is very important in retinal layer segmentation
- It’s width, \( m \) is often called the size of the *margin*
- It determines the architecture of your graph

Chiu et al., 2010

- Uses Dijkstra’s algorithm to traverse the cost images data
- Margin set to 1, with no smoothing penalty
- Cost images based on signed edges:
  - Dark to light image for segmenting a darker layer above a lighter layer
  - Light to dark image for segmenting a lighter layer above a darker layer

Chiu et al., 2010

- Dijkstra’s algorithm requires explicit setting of the start and end nodes
  - This requires adding columns either end of the image with zero cost
  - Alternative graph-traversal methods mitigate this problem

- Image must be pre-flattened to the curvature of the retina

Chiu et al., 2010

- Diagram showing layers of the retina with labels for each layer:
  - NFL: Nerve Fiber Layer
  - GCL: Ganglion Cell Layer
  - IPL: Inner Plexiform Layer
  - INL: Inner Nuclear Layer
  - OPL: Outer Plexiform Layer
  - ONL: Outer Nuclear Layer
  - IS: Inner Segment
  - OS: Outer Segment
  - RPE: Retinal Pigment Epithelium
  - Choroid

- Image showing a section of the retina with delineated layers.
LaRocca et al., 2011

- Robust automatic segmentation of corneal layer boundaries in SDOCT images using graph theory and dynamic programming, 1 June 2011 / Vol. 2, No. 6 / BIOMEDICAL OPTICS EXPRESS 1524

LaRocca et al.
LaRocca et al.

Yang et al. (Topcon)

Yang et al. "Automated layer segmentation of macular OCT images using dual-scale gradient information", 27 September 2010 / Vol. 18, No. 20 / OPTICS EXPRESS 21293
Yang et al. (Topcon)

- The original image is processed to create a series of cost images
- Different layers are then segmented such that the data is continually reduced
- Graph architecture not defined

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Fig. 2: Illustration of the complementary gradient information used for segmentation of the IPL/INL boundary. The size of the Gaussian kernel used in the Canny edge detector was 2, while the sigma of Gaussian kernel used in the axial gradient calculation was 4. The thresholds of the Canny edge detector were [0.1, 0.55, 0.8].

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Fig. 4: Results of a normal 3D vertical scan volume. NFL, GCC (from ILM to IPL/INL) and total retinal thickness maps (from ILM to OS/RPE) covered 5x5mm² area in which three B-scans (the 32nd, 64th and 96th images) of this volume were shown. T: temporal; I: inferior; N: nasal; S: superior.
Dynamic Programming – Shortest Paths

• Pros:
  – Efficient global optimization tools
  – Current state of art

• Cons:
  – Only suitable for 1d structures
  – Can’t handle bubbles or object boundaries in volumetric data
Graph-cuts – Boykov-Jolly 2001

Minimum cost cut can be computed in polynomial time (max-flow/min-cut algorithms)

http://www.csd.uoc.gr/~komod/ICCV07_tutorial/

Graph-cuts – Boykov-Jolly 2001

Incorporating prior information

Suppose $I^s$ and $I^t$ are given “expected” intensities of object and background

http://www.csd.uoc.gr/~komod/ICCV07_tutorial/
Garvin et al., 2008

Cost functions are developed using learned thickness distributions:


Shape modeling overview

- Prior knowledge of a structure or object can be learned and applied as a constraint
- Learn typical shapes
- Save time optimizing
  - Search only plausible shapes
Robust segmentation of intra-retinal layers in the normal human fovea using a novel statistical model based on texture and shape analysis.

Learn typical shapes/textures for layers on B-scans

- 26 points per layer, 8 layers per B-scan (208 total)
- 4 texture features per layer (32 total)
- Dimensionality reduction (208 -> 12, 32 -> 2)
CUP & DISC SEGMENTATION

The Cup and Disc make up the measurable parts of the Optic Nerve Head (ONH)

In the figure, the arrows point to:
1. End of RPE
2. Choroid and (3) sclera extend past the RPE to form a halo
3. The margin of Bruch’s membrane appears to extend past the scleral margin
4. Bruch’s Endpoint


- Segment the disc in 2d using an active contour
- Very difficult to choose appropriate parameters
- Likely to lock onto first feasible (local) result

http://www.gig.pitt.edu/Research3

Lee et al., 2010

Based on layers segmented within the OCT volume

Lee et al., 2010

- They axially derive features within the 3d volume, such that the areas of interest can be classified

Hu et al., 2010

- Moved to a graph-based approach, where the disc was explicitly segmented in a 2d image using a graph-based method
- The cup was then defined as the intersection of the plane with the vitreous interface

Hu et al., Automated Segmentation of Neural Canal Opening and Optic Cup in 3-D Spectral Optical Coherence Tomography Volumes of the Optic Nerve Head, Invest. Ophthalmol. Vis. Sci. 2010; 0: iovs.09-4838v1 iovs.09-4838
Hu et al., 2010

- Create a 2D image from the OCT volume by integrating in Z
- Restricting the integration range helps improve contrast at the disc
- Then segment the 2D image

Data courtesy of Robert Change MD, Stanford School of Medicine

Hu et al., 2010

- Segmentation performed on Cost Images in Polar Space
Was a tutorial at Miccai 2010

- Graph Algorithmic Techniques for Biomedical Image Segmentation
- Ophthalmic image analysis – 3D
  - Including segmentation of 11 layers in macular OCT, and optic nerve head segmentation, ONH layers, deep layers
  - Prof. Xiaodong Wu, Ph.D.
  - Prof. Mona K. Garvin, Ph.D.
  - Prof. Milan Sonka, Ph.D.

Patent Applications in this Domain


Intra-retinal Segmentation Algorithms

COMMERCIAL ADOPTION

Spectral/Fourier Domain OCT

http://www.wiley-vch.de/berlin/journals/op/09-04/OP0904_524-528.pdf
http://www.revoptom.com/content/796/c/14792/
Commercial Adoption

- Aside from Intellectual Property issues....
- Segmentations can take around an hour
  - Clinical use requires << 10 seconds per volume
- Adoption requires *clinical* studies verifying efficacy (accuracy)
  - FDA for claims and then Sales and Marketing will require these
- Adoption requires *clinical* studies verifying repeatability
  - Again to support claims to the FDA but also to sell the instrument

*In essence, this means clinical publications, where the algorithm is of less interest, but the clinical outcome is all important.

Optovue Inc.

- Optovue Inc., were the first to market with an automated *intra-retinal* segmentation algorithm
- The layer of interest being the posterior of the IPL
- This has value in Glaucoma, where the Ganglion Cell Layer thins

More recently, Carl Zeiss Meditec have developed their own inner retina segmentation algorithms. GC-IP thickness is the thickness between the yellow and magenta lines.

- Has already generated three journal publications:
  - “Primary retinal pathology in multiple sclerosis as detected by optical coherence tomography”, Brain, Accepted October 14, 2010
  - Since then, another Brain publication has been accepted as well as a submission to the Journal of Multiple Sclerosis
- Algorithm available commercially later this year
  - Carl Zeiss Meditec, Cirrus version 6.0

http://brain.oxfordjournals.org/content/134/2/518.short
Cup & Disc Segmentation Algorithms

COMMERCIAL ADOPTION

Heidelberg Cup & Disc Segmentation is based on confocal imaging.

Cup & Disc Segmentation
Optovue Inc., were again the first for the new OCT devices:

http://www.oct-optovue.com/images/rnfl.jpg
Cup & Disc Segmentation

Followed by Carl Zeiss Meditec Inc.

Is change pathological?

REGISTRATION
Algorithms for Ophthalmic Image Registration

• Registration useful for
  – Change analysis (intra-modality)
  – Image fusion (inter-modality)

• Algorithms
  – Landmark-based
  – Intensity-based

Change analysis: intensity-based

• Volumes are typically registered in 2d only
• 3d registration is an area of active research

Baseline VA 20/30+2


1.5 month post Avastin #4 VA 20/20

Change Analysis Software

Combination of Topcon 3D OCT & FA/FAF/ICG images and more
Autofluorescence, fluorescence angiography and indocyanine green image is simply imported to allow pin point registration to aid the diagnosis of RPE and choroidal changes

Fusion: automatic
Fusion: landmark-based

- OCT / fundus images
  - Strong landmarks
  - Helps correct OCT artifacts

Fusion: Selective Pixel Profiling™
OTHER APPLICATION DOMAINS

Cardiology

• Rapidly pushing IVUS out of the market for coronary artery pathology assessment
  — 10x better axial resolution and 3x faster

• Can accurately measure thickness of fibrous caps (vulnerable plaque)
  — Assessment of risk of rupture

Cardiology

- Image processing issues:
  - Lumen segmentation
  - Plaque characterization

Dermatology

- Very useful for certain pathologies
- Good agreement with histology
- Limited by depth penetration (<2mm)
Dentistry

• OCT is first modality in dentistry to do high-res imaging both “hard” tissue (teeth) and “soft” tissue (gums)
  – Detects decay before it shows up on X-ray

Non-medical

• OCT can be used for non-destructive testing of any layered materials
  – Art (right)
  – Chemical polishes
  – Foils
  – Bonding quality
FUTURE TRENDS

Hardware

• Steady evolution of the hardware
  – Faster cameras
  – Different wavelengths
  – Combo modalities
  – Lower costs, etc.
  – Cheaper components
“Ultrahigh speed 1050nm swept source / Fourier domain OCT retinal and anterior segment imaging at 100,000 to 400,000 axial scans per second”, 13 September 2010 / Vol. 18, No. 19 / OPTICS EXPRESS 20031
Benjamin Potsaid, Bernhard Baumann, David Huang, Scott Barry, Alex E. Cable, Joel S. Schuman, Jay S. Duker, and James G. Fujimoto

Fig. 7. (A) OCT fundus image of 3D volume acquired at 100kHz with 500x500 axial scans over 6mmx6mm (2.6 sec). (B) 100kHz cross sectional image. (C) 3D volume rendering of 100kHz data (Media 1). (D) OCT fundus image of 3D volume acquired at 200kHz with 700x700 axial scans over 6mmx6mm (2.6 sec). (E) 200kHz cross sectional image. (F) 3D volume rendering of 200kHz data. Images are cropped in depth to span 2mm.

Software

- Image Management Systems
  - Better electronic record systems and management
  - “Open Architectures”
- Image processing algorithms
  - The low hanging fruit in ophthalmology is perhaps gone
- But...

http://www.retinaphysician.com/article.aspx?article=103653
Analysis Algorithms

- Sophisticated methods are too slow, and not, therefore, clinically applicable
- The fast methods are not sophisticated enough to be accurately applied across all disease states
- Ideally you would want to take the best of both worlds from all algorithms we have seen
- A marriage of shape and graph-based methods can leverage both
- Careful reductionist techniques may yet make them execute at clinically realistic speeds
- Lower quality devices will soon be ubiquitous, so the analysis tools offered will be a key differentiator
- Ultimately clinical usage is based on analysis performance

Thank you!

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- [http://www.springerlink.com/content/386552t20738t268/](http://www.springerlink.com/content/386552t20738t268/)
- Images: Gambichler, et al. 2011
- Images: www.LantisLaser.com
- Images: Liang, et al., 2011

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