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Geometric morphometric analysis

for quantifying and categorizing brain structure shape in diabetic and non-diabetic populations

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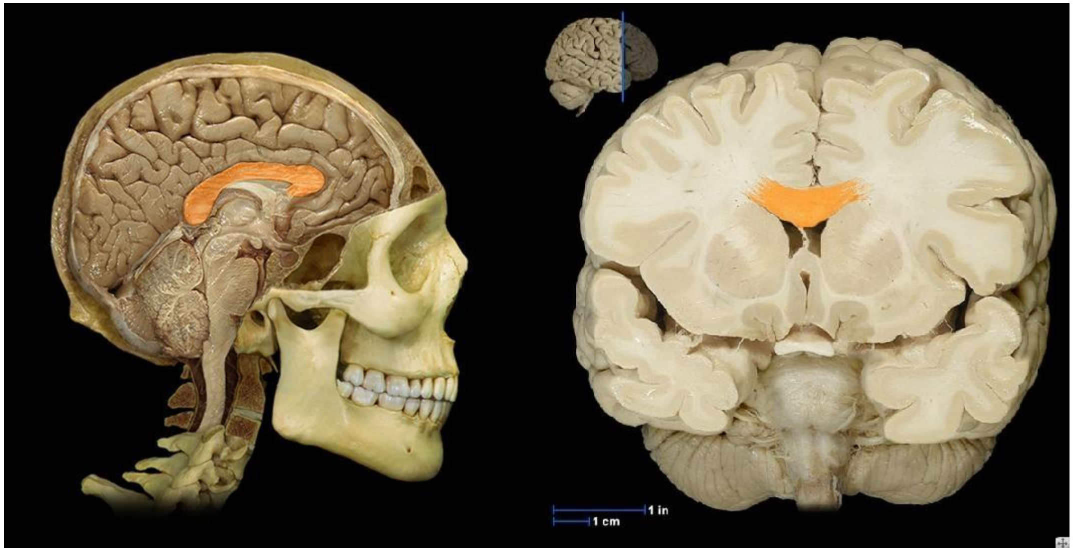
Australian National University

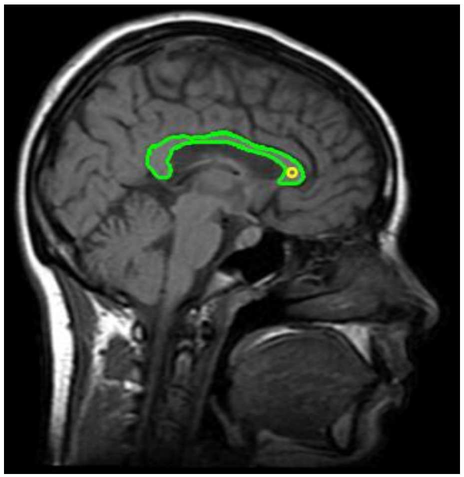
Shape can impact function

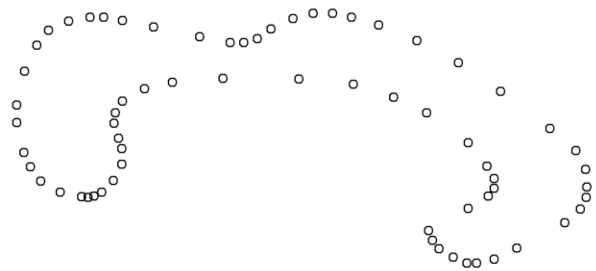


Sources: http://www.previninc.com/shop/media/detail/93433.jpg
http://www.matferbourgeatusa.com/content/images/thumbs/0001141_mise-en-bouche-mini-bent-spoon.jpeg
http://img.photobucket.com/albums/v120/tanalu/Spoon4.jpg
http://johnlewis.scene7.com/is/image/JohnLewis/231159253?$prod_exlrg$http://femininepeace.org/wp-content/uploads/corpus_callosum1337487504159.jpg

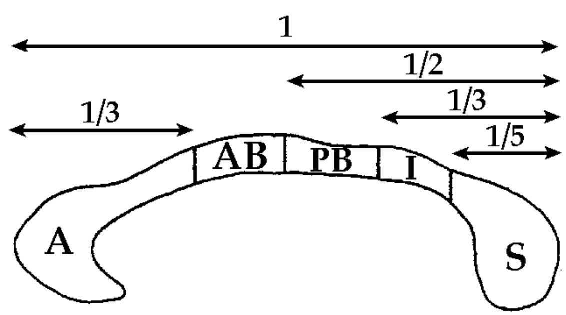
How to quantify shape?

A problem of dimension reduction





glm(Diabetes ~ area)



glm(Diabetes ~ areaA)
glm(Diabetes ~ areaAB)
glm(Diabetes ~ areaPB)

Geometric morphometric analysis

glm(Diabetes ~ shape)?

Source: http://cmp.felk.cvut.cz/cmp/demos/Medical/LevelSetSegmentation/images/corpusCallosum_seg.jpg

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How to quantify shape?

Polygons and fouriers

Polygonisation

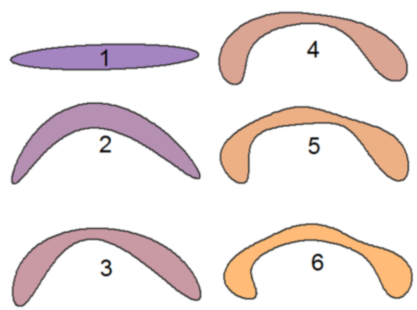
- Deconstruction of shape into polygons (here, rectangles)

Simplified coordinates

	x	y
1	1.499993	0.7500055
2	1.331718	0.8540184
3	1.163443	0.9391722
4	0.995168	0.9900272

Fourier

- Deconstruction of shape into harmonics



Harmonics

A1	A2	A3	B1	B2	B3
1	0.0384	-0.00559	5.39e-17	0.0758	-0.0197
1	0.0473	-0.07230	-2.67e-17	0.0674	-0.0275
1	0.0587	0.00156	-4.89e-17	0.0546	-0.0174
1	0.0714	-0.03920	-5.25e-17	0.0887	-0.0357
1	0.0248	0.02420	0.00e+00	0.0522	-0.0111
1	0.0277	0.02920	1.62e-16	0.0558	-0.0317

eFourier

tFourier, rFourier

Sources: http://soccernewsday.com/userfiles/images/02-17-2012.jpg
http://f.tqn.com/y/quotations/1/W/h/D/173341886.jpg

How to quantify shape?

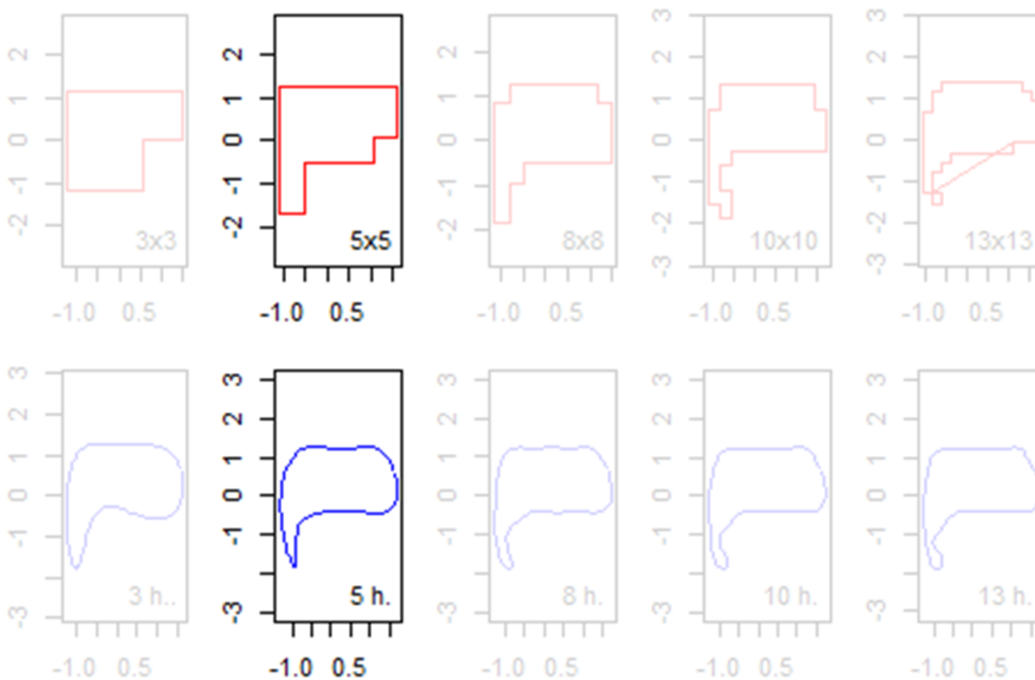
Polygons and fouriers

To get a little, you need to give a little…

Polygons
Variable dimension reduction
- 3x3 grid -> 6-9 coordinates
- 13x13 grid -> 6-169 coordinates

eFourier
Consistent dimension reduction
- 3 harmonics -> 6 harmonic pairs
- 13 harmonics -> 26 harmonic pairs

For this talk, we're going with **5**
- 5x5 grid -> 6-25 coordinates
- 5 harmonics -> 10 harmonic pairs



So, what works best?

… Wait, what is *'best'*?

What I've got:
How well the different methods can recover shapes

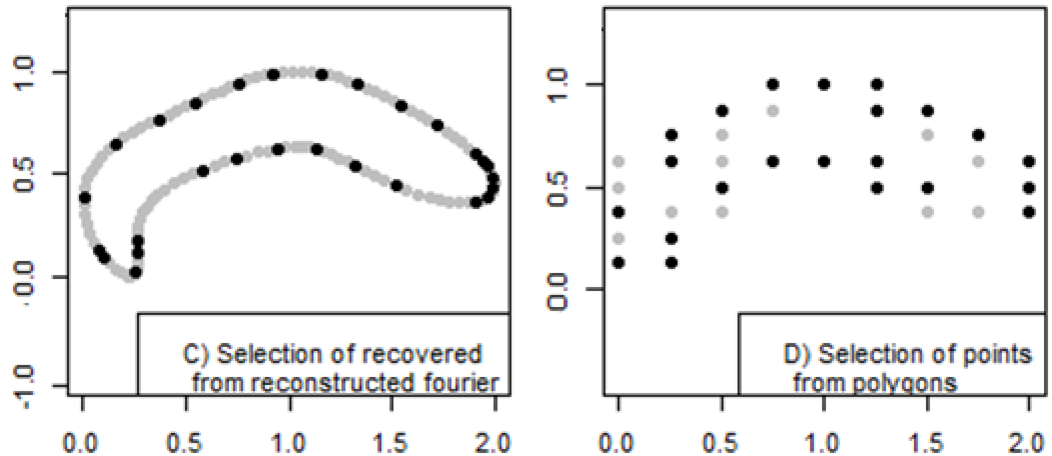
What I also want:
How sensitive the methods are to shape differences when plugged into subsequent (epidemiologist friendly) analyses

Source: http://www.theblaze.com/wp-content/uploads/2013/08/600x4503.jpg
http://georgiamidwife.org/wp-content/uploads/2015/07/We-want-you-image.png

Metrics for evaluation

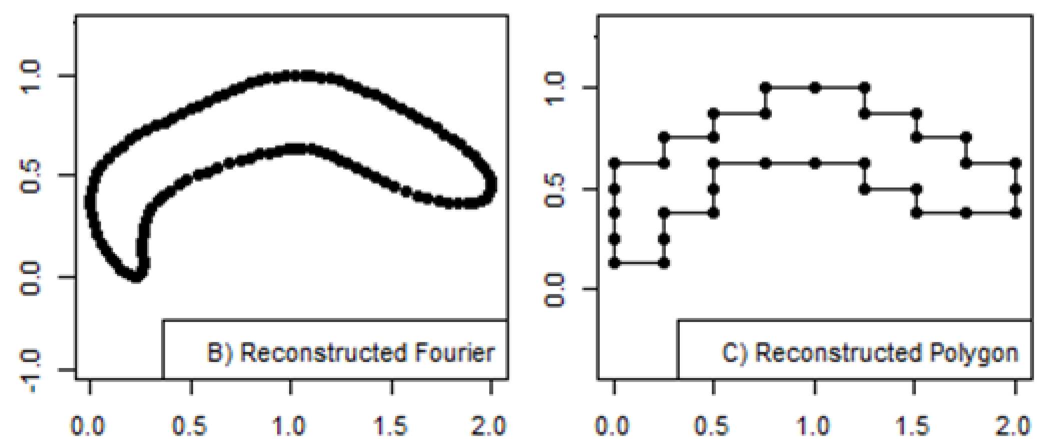
$$\frac{\sum_{k=1}^{K}\sum_{j=1}^{J}|Original_{kj} - Reconstructed_{kj}|}{K}$$

Outline fidelity



$$|Original_a - Reconstructed_a|$$

Area fidelity



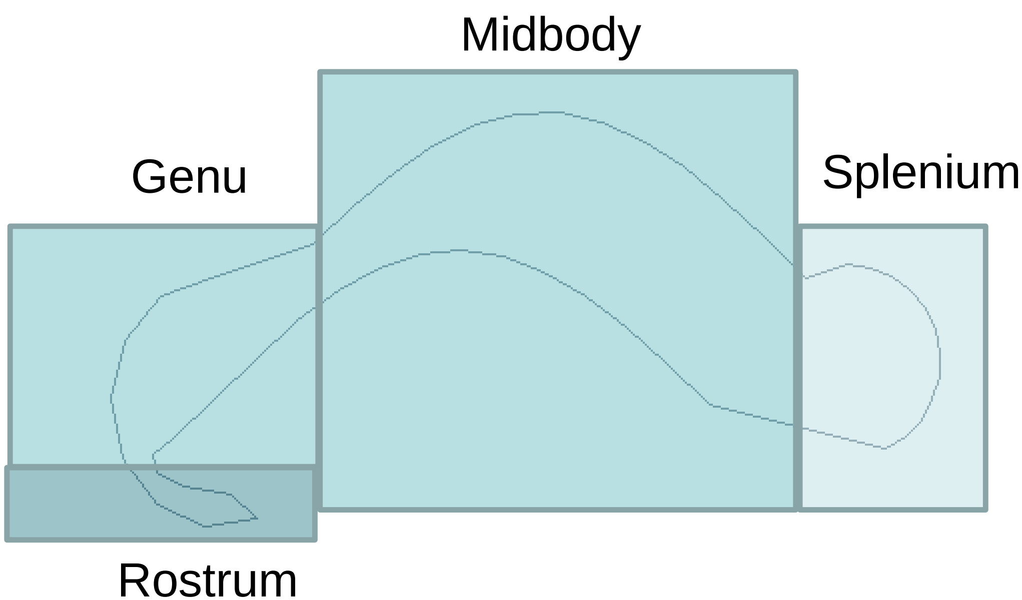
Shapes for evaluation

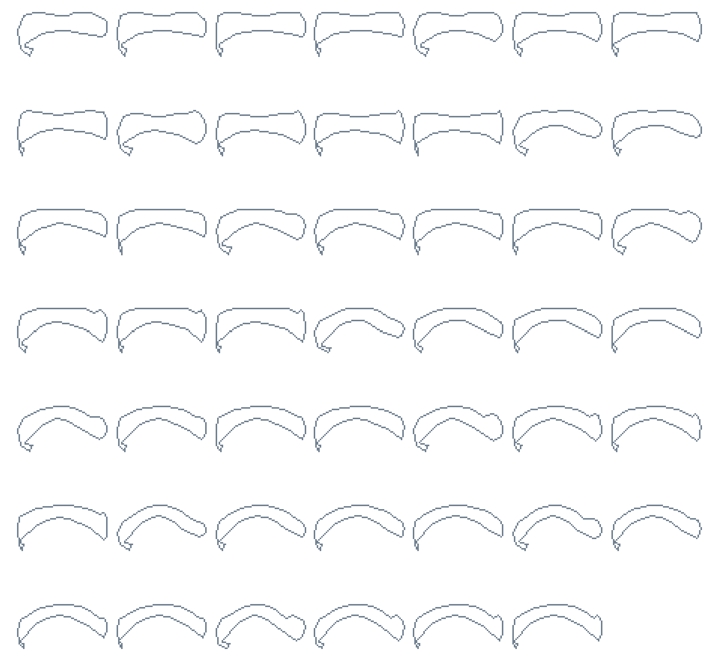
A lot of variability in ‘real’ data… so we’ll start with some fake data.

- Systematically modifiable test shapes with similar elements to the corpus callosum

Caveat: WITHOUT using tools we will then use to describe the shapes

- – Solution: Frankenstein’s monster of circles and sine waves:

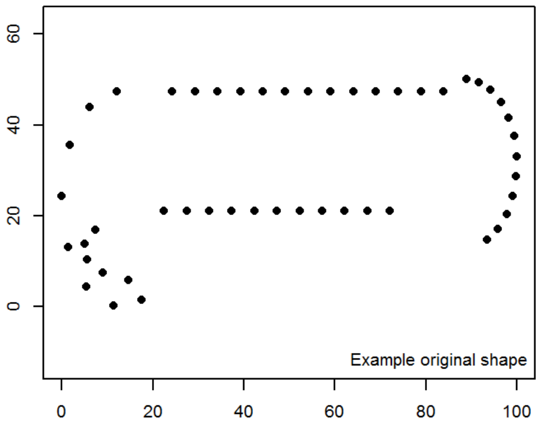




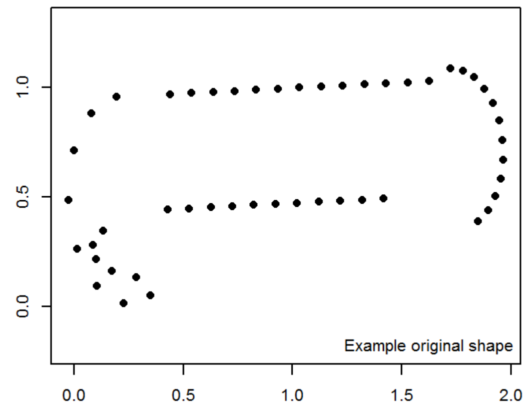
Modification of things that shouldn't change…

Non-shape differences

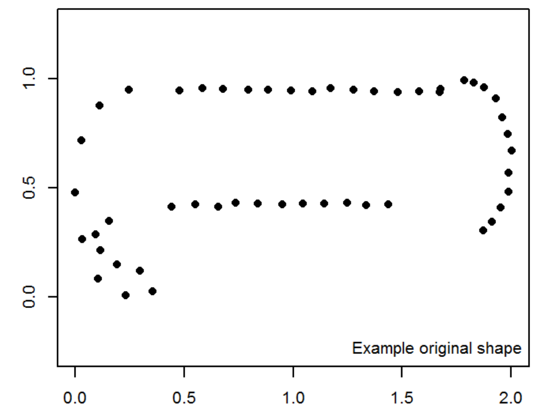
Scale



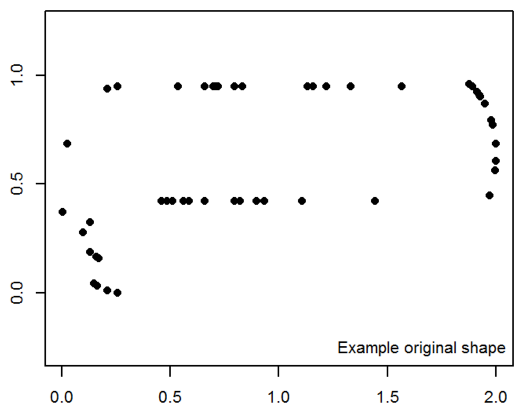
Orientation



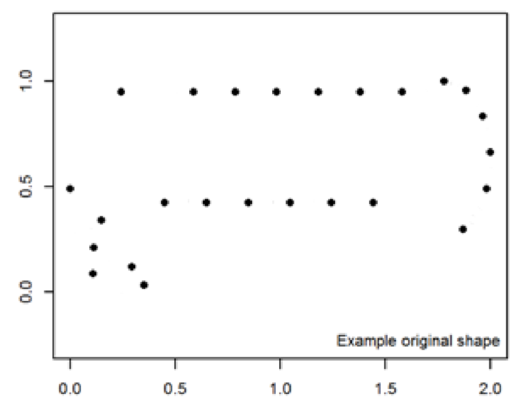
Jitter in outline



Randomness in outline



Number of points



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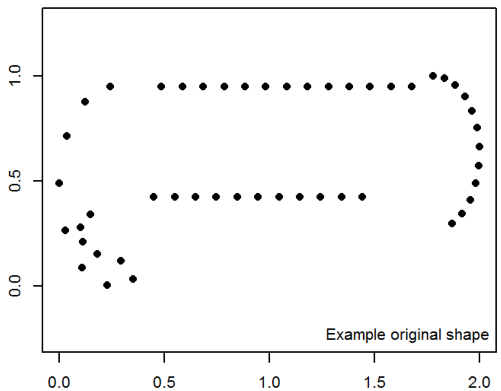
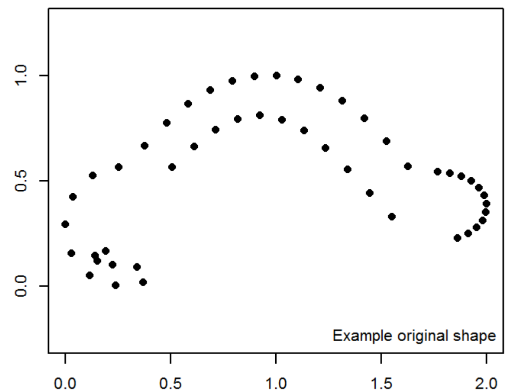
Modification of things that should change….

Real shape differences

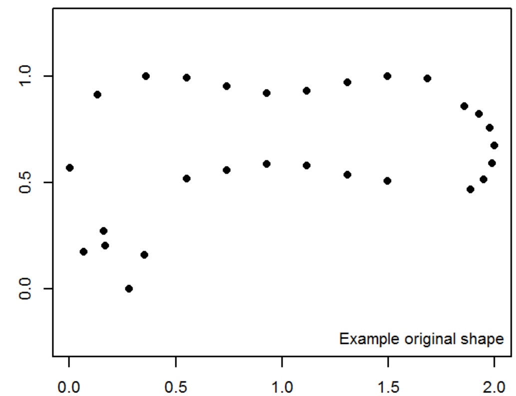
Length



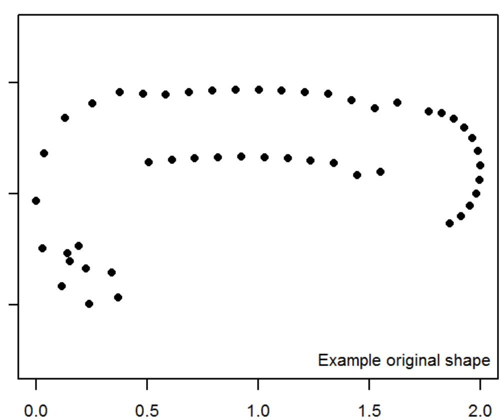
Curve



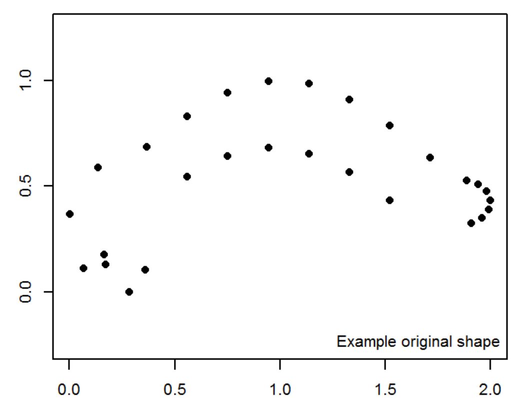
Regularity



Splenium size



Everything changing!



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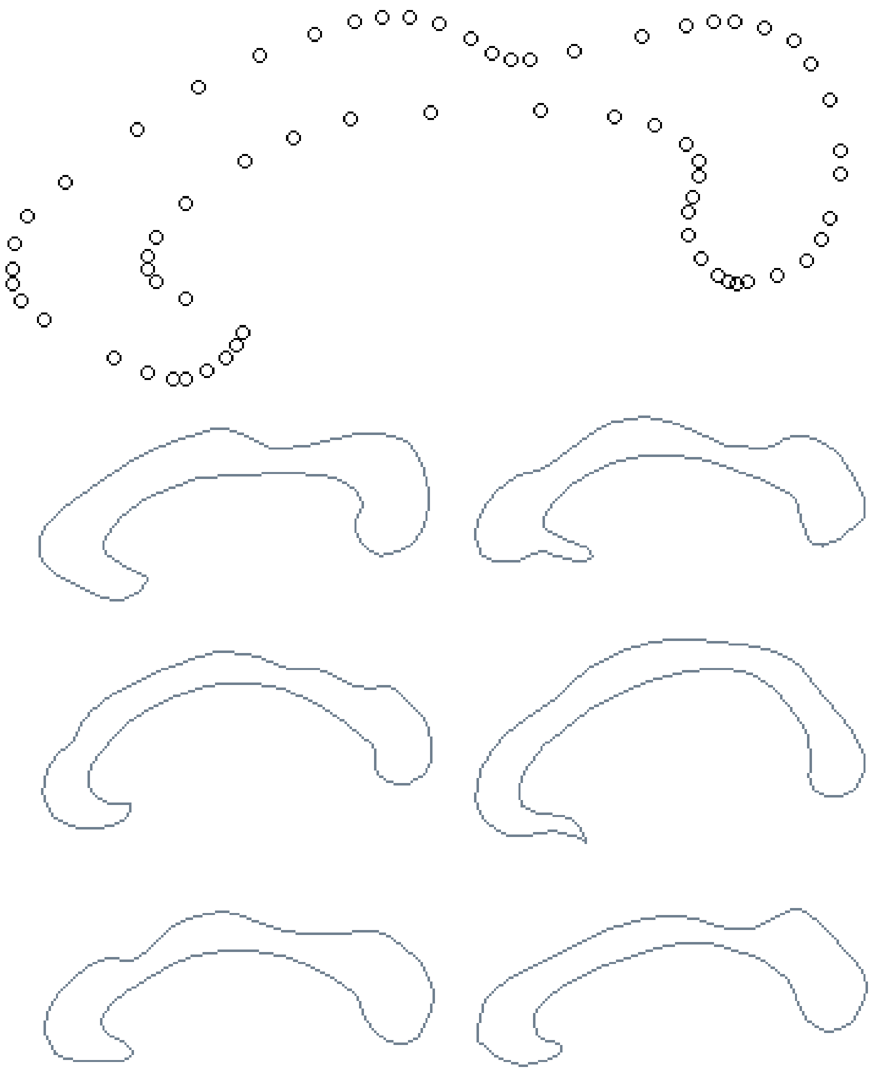
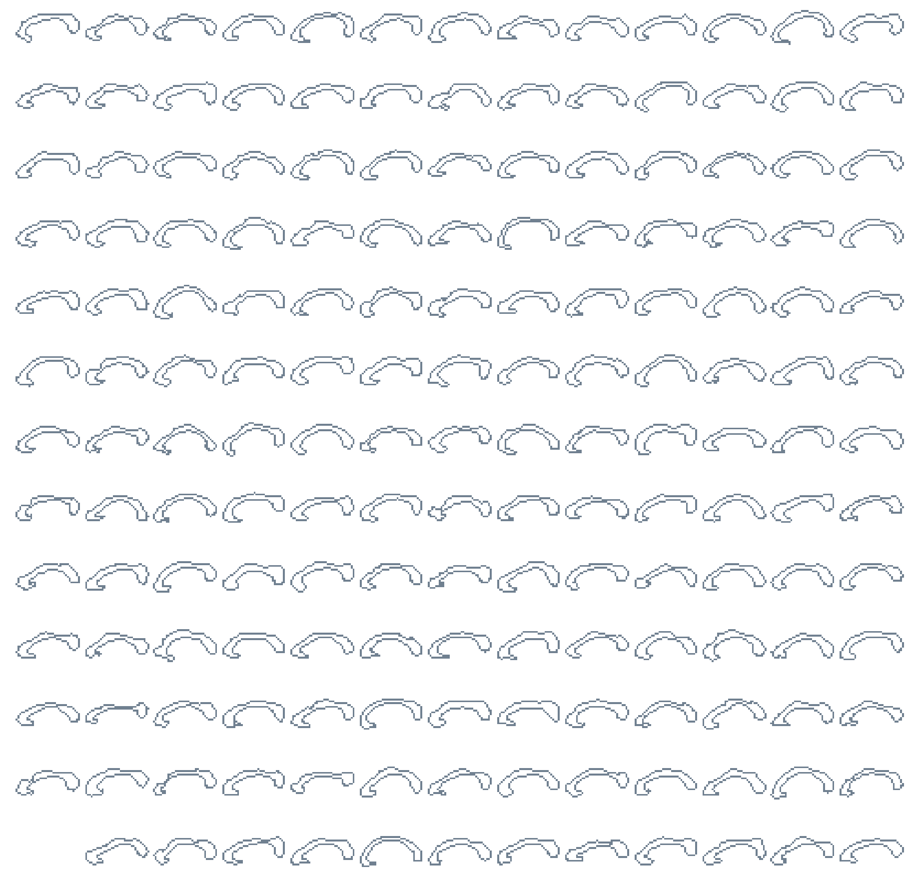
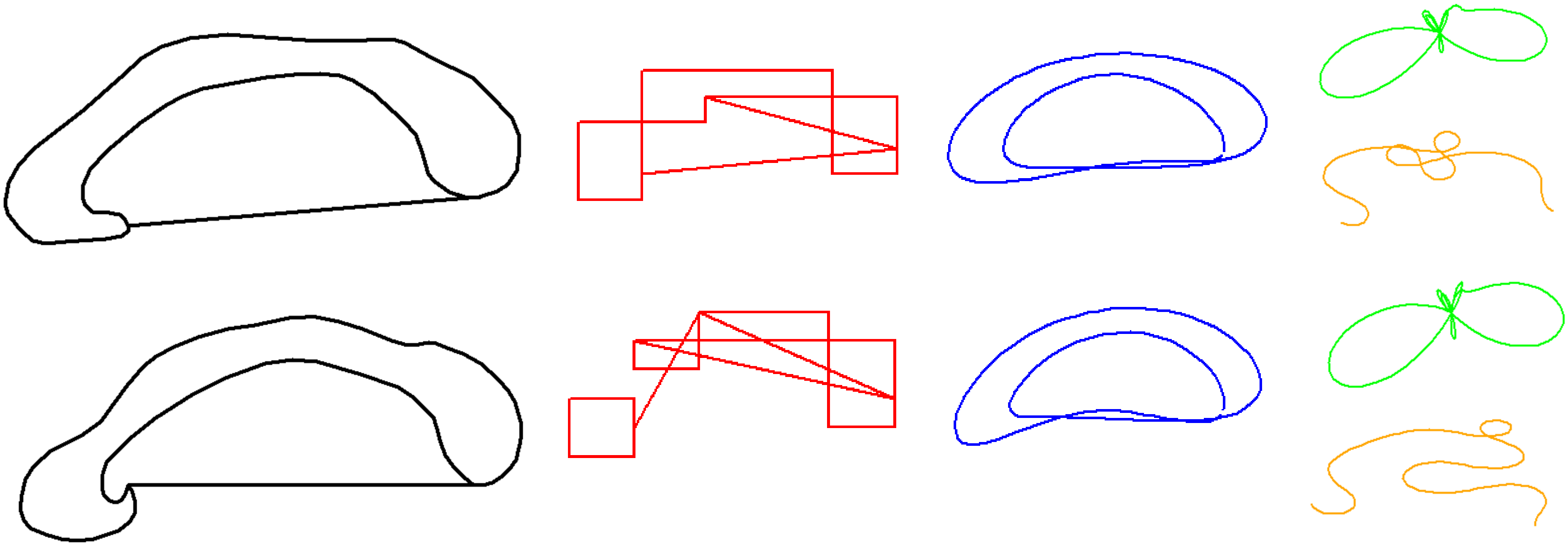
… then try it with the real thing.



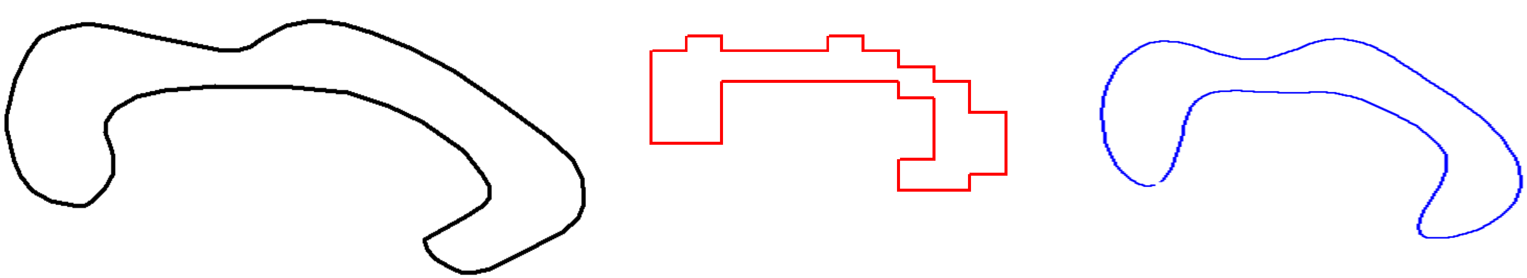


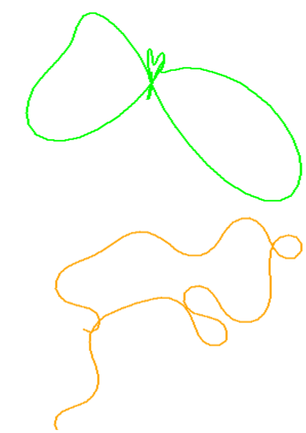
168 traces
Community-living adults from the PATH Study.

The eyeball test



… Ramp up the detail + clean up input shape

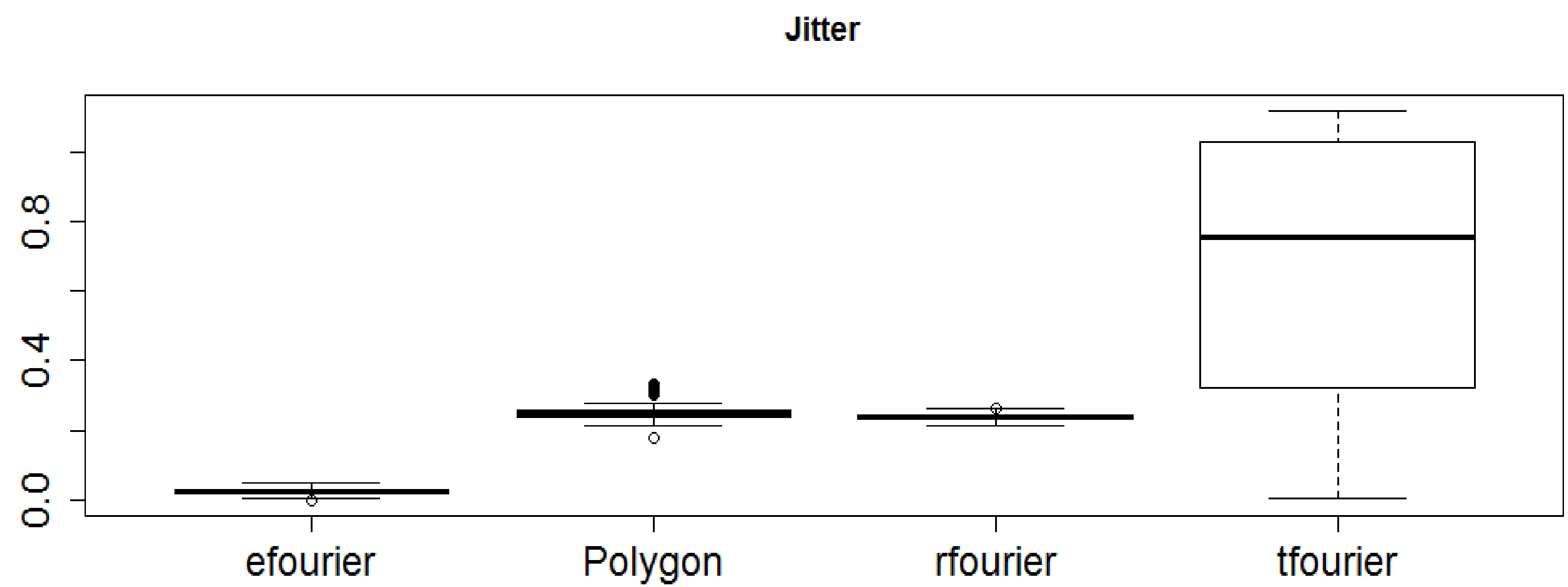




Quantifying ‘best’

Fidelity of area reconstruction $|Original_a - Reconstructed_a|$

glm(area difference ~ method) Smaller-is-better	(Intercept)	Polygon	rFourier	tFourier
Multiple parameters	0.04 [0.02,0.05]	0.6 [0.58,0.62]	0.29 [0.28,0.31]	0.21 [0.2,0.23]
Real data				
Real Shapes	[illegible] [196.18,309.07]	[illegible] [755.74,915.4]	1065 [985.17,1144.83]	1067.75 [987.92,1147.59]



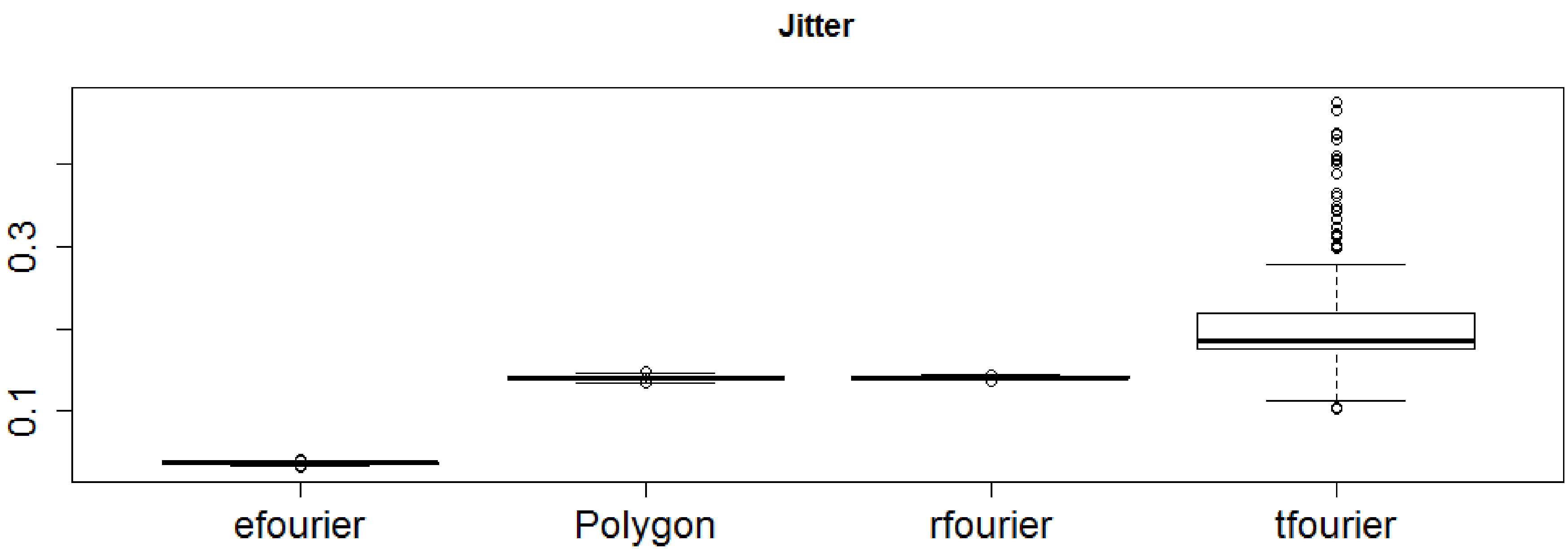
Interpretation: everything is worse than e-fourier

Base group: eFourier. Harmonics: 5, grid: 5x5. n=1000, except for real shapes (n=168). [denotes 95% CI.

Quantifying ‘best’

Fidelity of outline reconstruction $$\frac{\sum_{k=1}^{K}\sum_{j=1}^{J}|Original_{kj} - Reconstructed_{kj}|}{K}$$

glm(outline difference ~ method) Smaller-is-better	(Intercept)	Polygon	rFourier	tFourier
Real data				
Real Shapes	[illegible]	[illegible]	[illegible] [2.28,2.51]	3.37 [3.25,3.48]

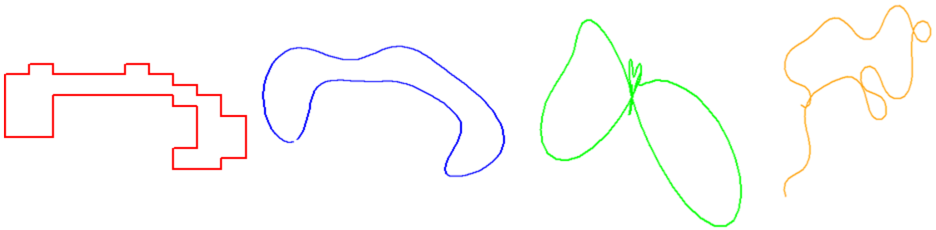


Interpretation: everything is worse than e-fourier

Base group: eFourier. Harmonics: 5, grid: 5x5. n=1000, except for real shapes (n=168). [denotes 95% CI.

All signs point to…

- Fidelity of outline reconstruction
- Fidelity of area reconstruction



Quantifying ‘best’

Q: How to quantify sensitivity to shape differences?

e.g. If I systematically modify the size of the splenium, at what point does the method register the difference?

(binary and/or continuous outcomes)

Source:
http://img2.wikia.nocookie.net/__cb20121213183536/es.pokemon/images/3/38/EP768_Leavanny_debilitado.png

The goal:

Quantify and categorize corpus callosum shape in diabetic and non-diabetic populations.

The question:

How best to quantify shape?

The (provisional) answer:

eFourier analysis

The next step:

- Better evaluation *sensitivity* to shape
  (Q: If I systematically modify the size of the splenium, at what point does the method register the difference?)
- eFourier frolic
  (Q: any interesting suggestions beyond MANOVA and PCA?)

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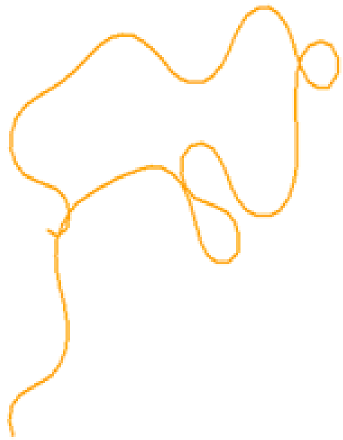
Acknowledgements

Thanks to:

- N. Cherbuin, M. Shaw, M. Fraser, the PATH team, interviewers and participants (for the data)
- V. Bonhomme (for the Fourier analysis r package that made all this practical)
- The Australian Research Council, Australian National Health and Medical Research Council, and National Infrastructure Facility (for the funding)

Happy to share R spaghetti code underlying this talk!



Bonus conclusion: rFourier = spaghetti?

We want YOU to suggest…

- Better evaluation *sensitivity* to shape
  (Q: If I systematically modify the size of the splenium, at what point does the method register the difference?)
- eFourier frolic
  (Q: any interesting suggestions beyond MANOVA and PCA?)

Stuff that didn’t fit in the presentation

Things to do

- (intended) full list of comparisons:
  - Constructed
  - Real (manually traced)
  - Real (automatically traced)
- Other similarity tests
  - Presence/absence of vectorized pixle in raster space (typically used in neuro for inter-rater reliability for area traces)
    - Jaccard index
    - Sørensen–Dice coefficient
  - ICC instead of glm

- Possible sensitivity tests
  - Sample output from 1000 shapes, 100 per group, increase distance between groups, GLM until significance
  - Simulate binary or continuous correlates for shapes, see how big the correlate has to be before GLM picks out a predictive relationship

- Poor tFourier and rFourier
  - Re-run with re-sampled contours so their assumptions are met so they have a fighting (if unrealistic) chance

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Numeric results

Fidelity of area reconstruction

$$|Original_a - Reconstructed_a|$$

glm(area difference ~ method) Smaller-is-better	(Intercept)	Polygon	rFourier	tFourier
Things which shouldn't change				
Scale	7637.48 [-2663.31,17938.27]	73587.84 [59020.33,88155.36]	67581.88 [53014.36,82149.39]	347059.85 [332492.34,361627.37]
Orientation	0.03 [0.02,0.05]	1.07 [1.05,1.08]	0.1 [0.08,0.11]	1 [0.99,1.02]
Jitter in outline	0.02 [0.01,0.03]	0.22 [0.21,0.24]	0.21 [0.2,0.23]	0.67 [0.66,0.69]
Randomness in outline	0.04 [0.02,0.06]	0.51 [0.48,0.53]	0.2 [0.18,0.23]	0.77 [0.74,0.79]
Number of points	0.03 [0.02,0.05]	1.07 [1.05,1.08]	0.1 [0.08,0.11]	1 [0.99,1.02]
Things which should change				
Midbody length	0.04 [0.03,0.05]	0.75 [0.73,0.76]	0 [-0.02,0.01]	0.58 [0.56,0.59]
Midbody curve	0.01 [0,0.03]	0.59 [0.57,0.61]	0.34 [0.32,0.36]	0.09 [0.07,0.11]
Midbody regularity	0.01 [0,0.02]	1.11 [1.1,1.12]	0.16 [0.15,0.17]	0.41 [0.4,0.42]
Splenium size	0.11 [0.09,0.12]	0.93 [0.91,0.95]	0 [-0.02,0.02]	0.52 [0.5,0.54]
Multiple parameters	0.04 [0.02,0.05]	0.6 [0.58,0.62]	0.29 [0.28,0.31]	0.21 [0.2,0.23]
Real data				
Real Shapes	252.62 [196.18,309.07]	835.57 [755.74,915.4]	1065 [985.17,1144.83]	1067.75 [987.92,1147.59]

Base group: eFourier. Harmonics: 5, grid: 5x5. n=1000, except for real shapes (n=168). [denotes 95% CI.

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Numeric results

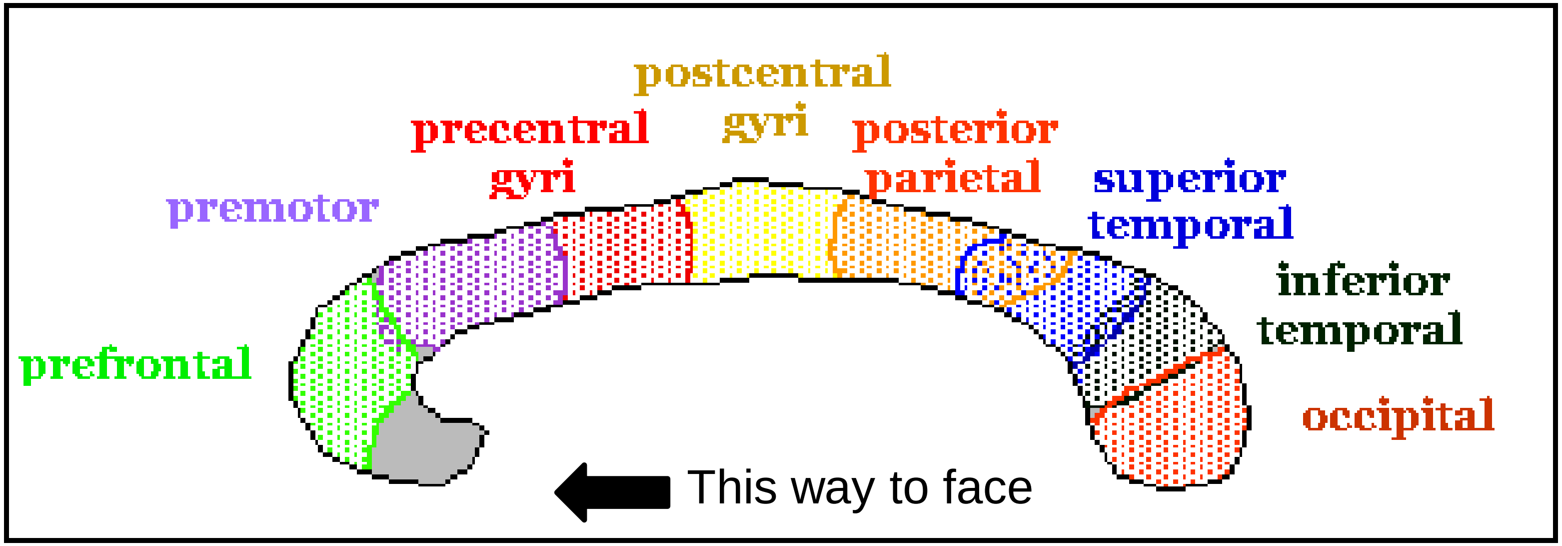
Fidelity of outline reconstruction $\frac{\sum_{k=1}^{K}\sum_{j=1}^{J}|Original_{kj} - Reconstructed_{kj}|}{K}$

glm(outline difference ~ method) Smaller-is-better	(Intercept)	Polygon	rFourier	tFourier
Things which shouldn't change				
Scale	18.24 [15.18,21.3]	51.58 [47.25,55.91]	52.99 [48.66,57.32]	119.72 [115.39,124.05]
Orientation	0.04 [0.04,0.04]	0.14 [0.13,0.14]	0.09 [0.08,0.09]	0.2 [0.2,0.2]
Jitter in outline	0.04 [0.04,0.04]	0.1 [0.1,0.11]	0.1 [0.1,0.11]	0.16 [0.16,0.16]
Randomness in outline	0.04 [0.04,0.04]	0.1 [0.09,0.1]	0.09 [0.09,0.1]	0.19 [0.19,0.2]
Number of points	0.04 [0.04,0.04]	0.1 [0.1,0.1]	0.07 [0.07,0.08]	0.17 [0.17,0.17]
Things which should change				
Midbody length	0.05 [0.04,0.05]	0.1 [0.1,0.11]	0.08 [0.08,0.08]	0.17 [0.17,0.17]
Midbody curve	0.04 [0.04,0.04]	0.11 [0.1,0.11]	0.07 [0.07,0.07]	0.09 [0.09,0.09]
Midbody regularity	0.04 [0.04,0.04]	0.1 [0.1,0.1]	0.09 [0.09,0.09]	0.16 [0.16,0.16]
Splenium size	0.05 [0.05,0.05]	0.1 [0.1,0.1]	0.08 [0.08,0.08]	0.15 [0.15,0.15]
Multiple parameters	0.04 [0.04,0.04]	0.1 [0.1,0.1]	0.08 [0.08,0.08]	0.12 [0.12,0.12]
Real data				
Real Shapes	1.69 [1.61,1.77]	3.31 [3.19,3.43]	2.39 [2.28,2.51]	3.37 [3.25,3.48]

Base group: eFourier. Harmonics: 5, grid: 5x5. n=1000, except for real shapes (n=168). [denotes 95% CI.

Corpus callosum connectivity

- Caveat: thicker doesn't always mean more connections (it also depends on how densely packed it is)
- **Approximate** locations of connections to neural regions



Davis, K. L., Libon, D. J., Nissanov, J., Skalina, S. M., Lamar, M., & Chute, D. L. (1999). Neuropsychological assessment and volumetric magnetic resonance imaging of the corpus callosum in dementia. *Archives of Clinical Neuropsychology*, *14*(8), 622-623.