The shape of thought: data-driven synthesis of neuronal morphology and the search for fundamental parameters of form

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Introduction

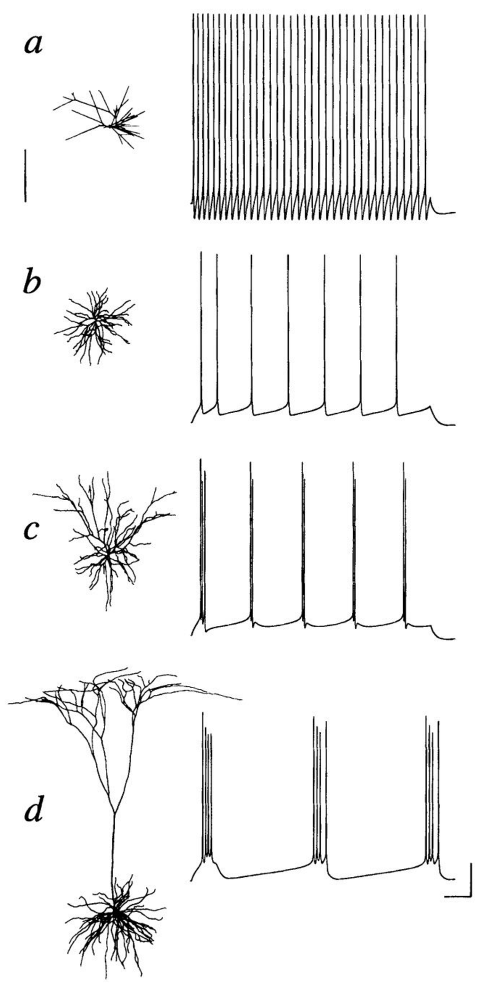
Neuronal morphologies are essential for bio-physically realistic computational modeling:

- Morphology determines connectivity
- Morphology influences electrophysiology
- Diversity required for robustness

Experimental reconstruction of neuronal morphology has limitations:

- Time-consuming and labor-intensive
- Small numbers and lack of scalability
- Incompleteness and artefacts

Data-driven computational synthesis of "virtual" morphologies has the potential to overcome these limitations.



Background

Hillman (1979) proposed that "from the mass of quantitative information available" a small set of "**fundamental parameters of form**" and their intercorrelations could be measured from reconstructed neurons which could potentially "completely describe" the population.

Thought the parameterization should be:

- Easily measurable from reconstructions
- Consistent with and meaningful to electrophysiology
- Useful for comparing different neuronal types
- Complete and non-redundant

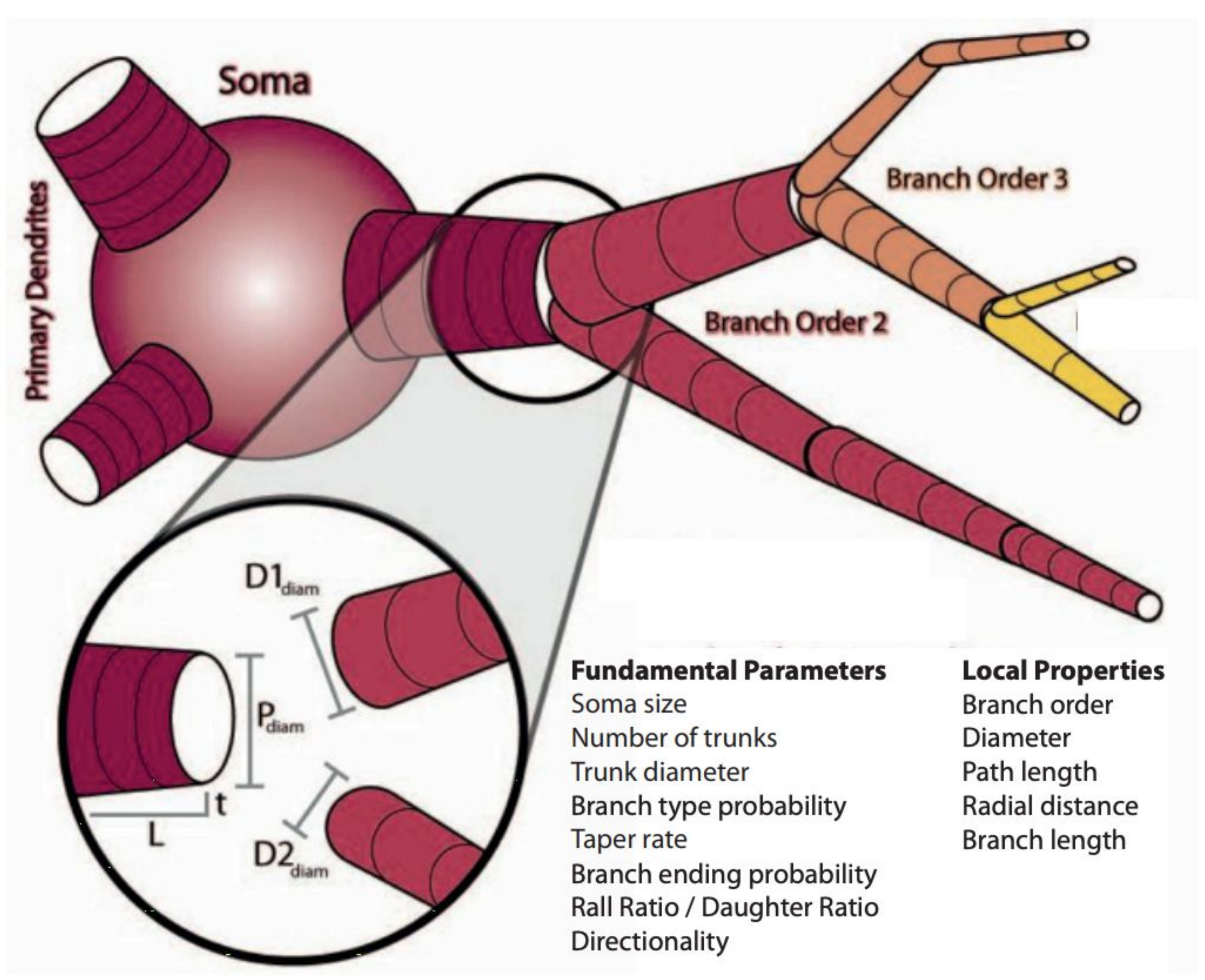
Burke et al. (1992) realized that virtual dendritic trees could be generated by stochastic sampling from a set of fundamental parameters (a synthesis model). Persistent differences between the reconstructed and virtual trees guided model refinement.

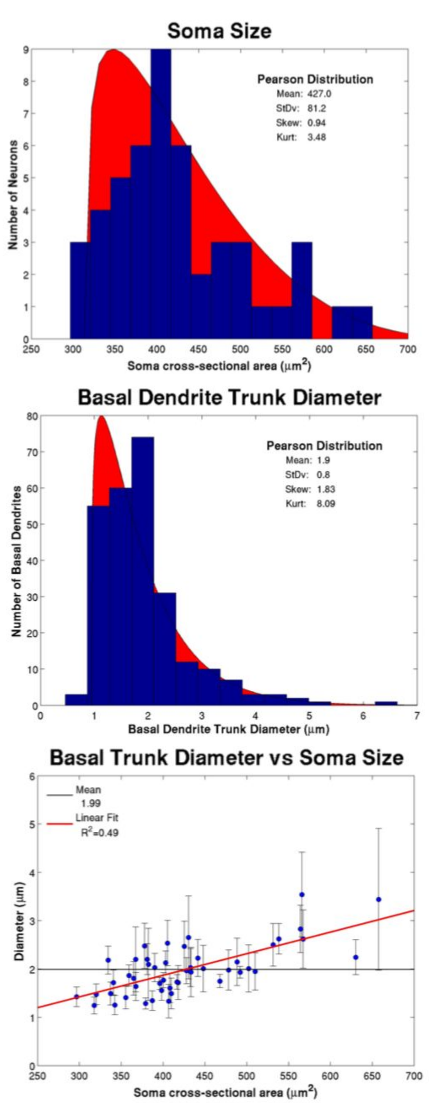
Ascoli et al. (2001) realized entire virtual neurons could be created by synthesizing multiple dendritic trees from a virtual soma. Ascoli et al. implemented the models of Hillman and Burke et al. and made the code and data publicly available.

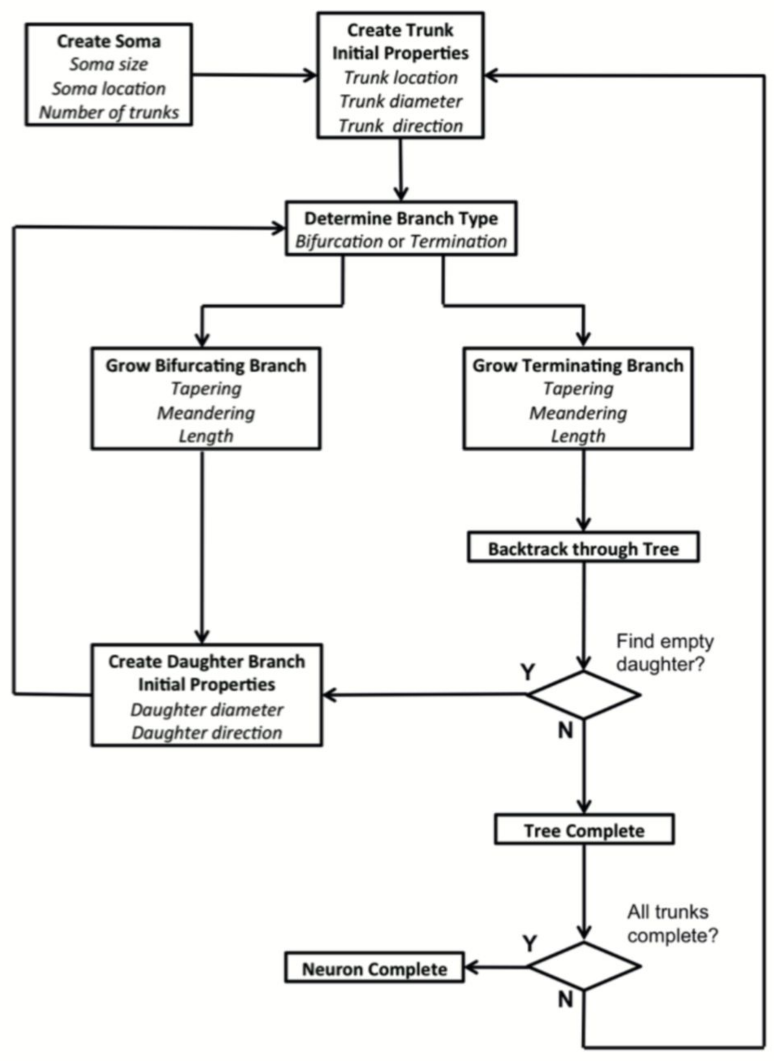
Both groups used the same data set: a population of six reconstructed cat alpha motoneurons. They were able to generate virtual motoneurons that were similar to the reconstructed ones, however, persistent, significant differences remained unexplained.

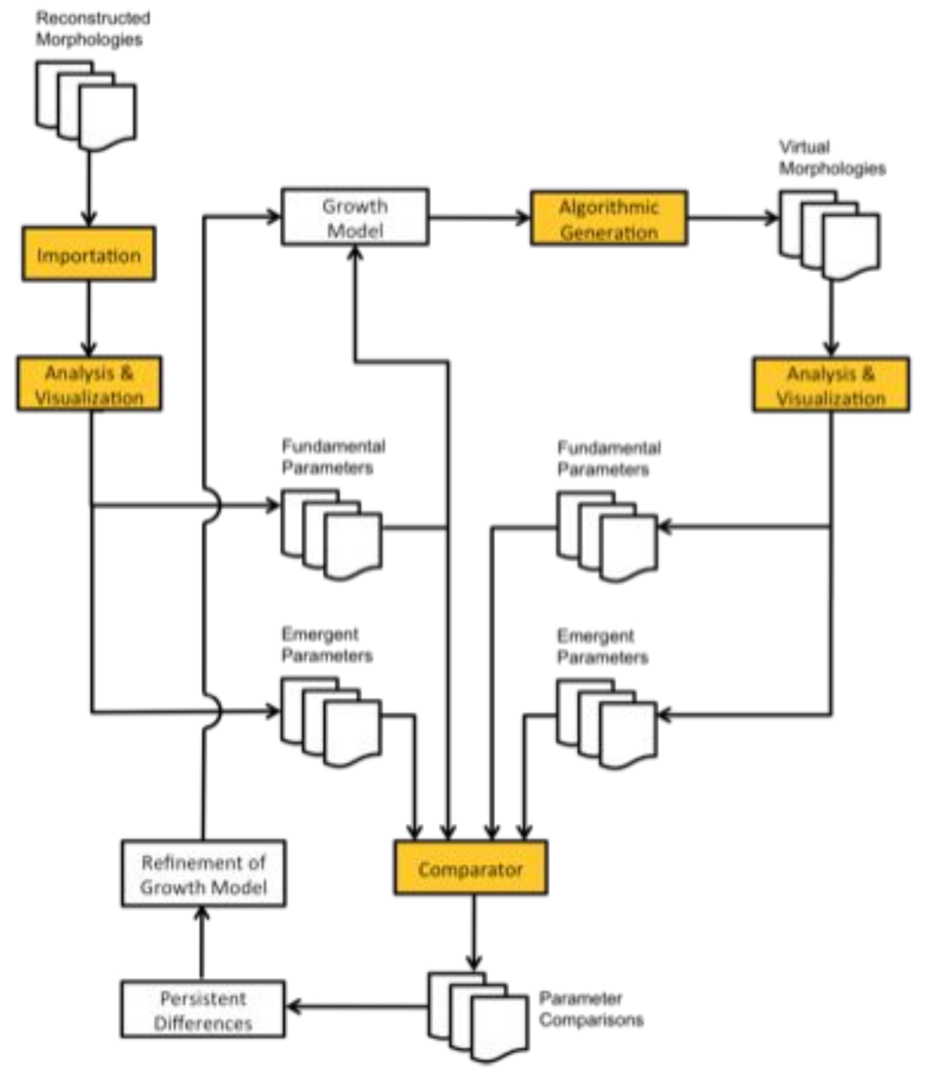
Methods (custom Matlab code)

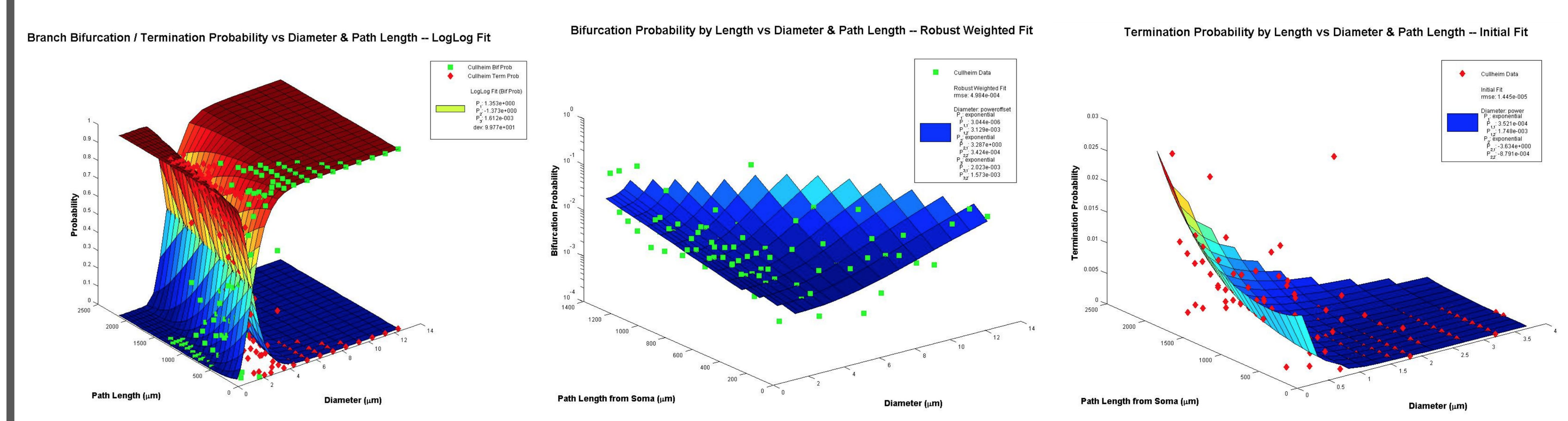
Parameterize neuronal morphology
Analyze parameters in a reconstructed population
Develop growth model of parameter relationships
Synthesize populations of virtual morphologies
Compare virtual/reconstructed morphologies
Refine growth model using persistent differences
Repeat synthesis / comparison / refinement cycle









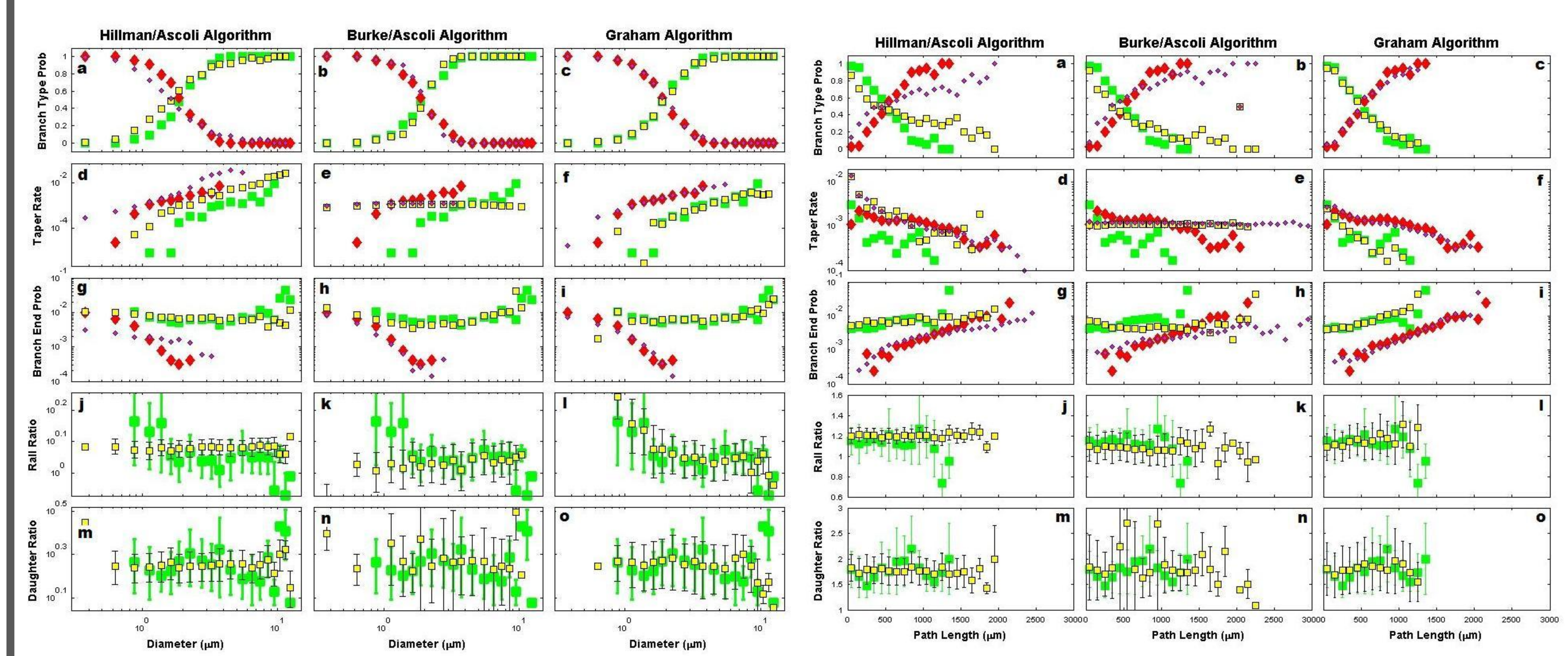


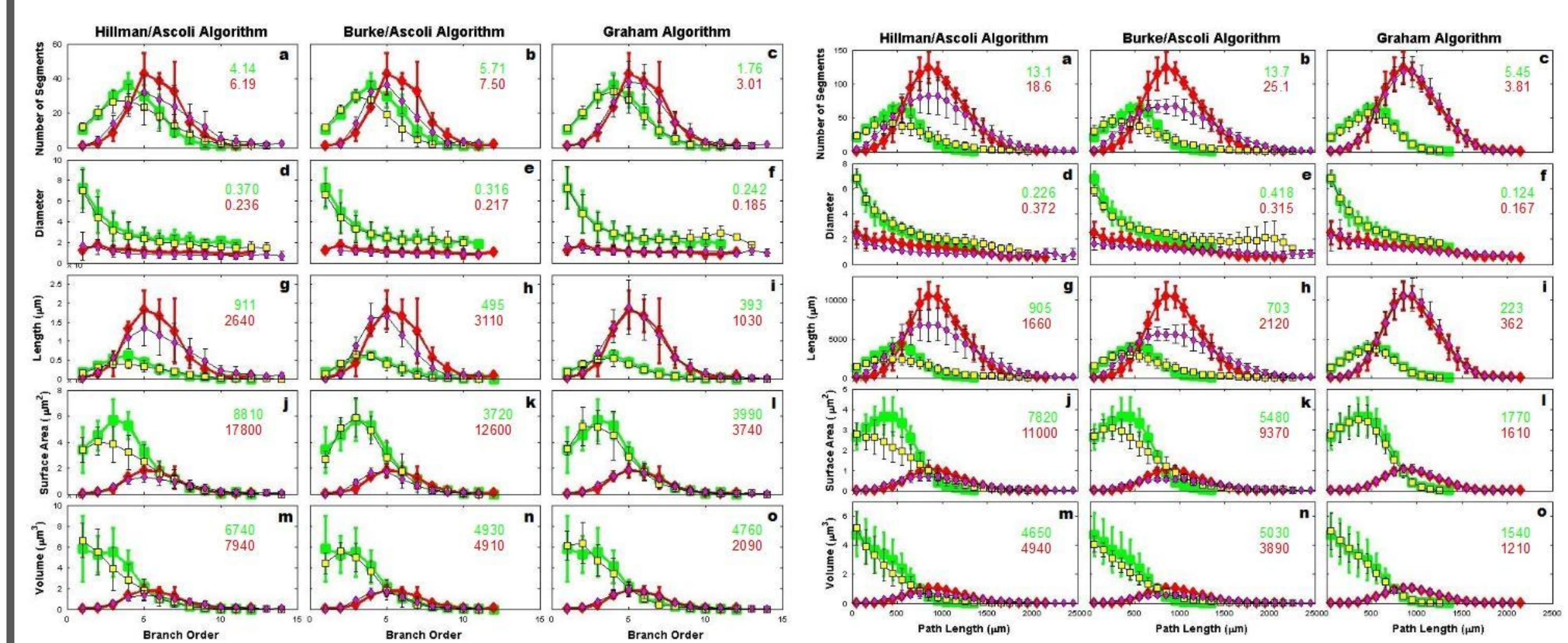
Results

Two major insights that improve synthesis:

- Parameters correlate with local properties, esp. diameter
- Parent branches and terminal branches behave differently

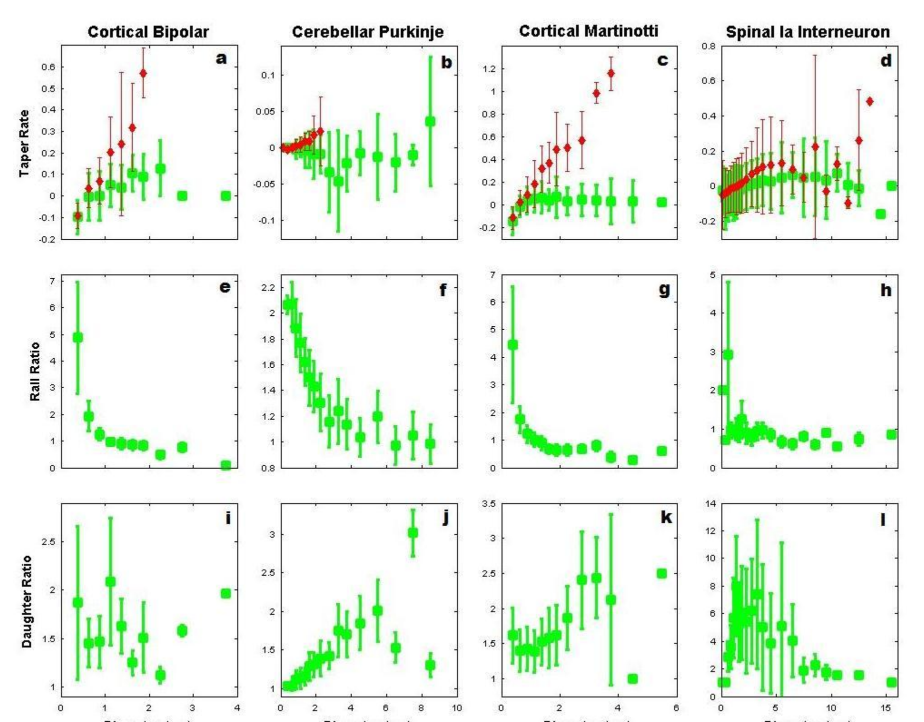
These insights hold true across a wide range on neuronal types





Future Steps

- Publish this work, release Matlab code (mnTools)
- Apply for funding / find job
- ***Pneumagtk***: Python Neuronal Morphology Analysis and Generation Tool Kit
- Sparse matrix representation
- Automate parameter space search (evolutionary algorithm?)



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