GROGRA and GENESIS: *in computo* grown neurons used for realistic compartmental modeling

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Abstract

We report on the novel use of the existing growth grammar interpreter GROGRA for neuroanatomical simulations of pyramidal cells, interneurons and purkinje cells. Growth parameters for these cell types result from analyzing web-based cell reconstructions by means of a custom made Matlab-program and corroborate existing literature data. Synthetic cells are displayed and studied in a VRML-browser. GENESIS simulations of several sets of synthetic morphologies are then used to shed light on the question, how much influence morphology needs to have in a truly realistic network simulation.

Key words

GROGRA, neuroanatomical modeling, compartmental modeling, GENESIS, VRML, network modeling

Introduction

Our recently introduced GENESIS model of a small part of the CA3 region of the rats brain [6] contains at least one very significant difference to its real biological counterpart: All its 72 pyramidal cells and the 18 interneurons are clones of single cells defined earlier by Traub [8-10].

The question arises, whether the response of this small network would change at all or even improve closer to biological reality, if all the cells would be modeled individually and not as cloned and coarse approximations. Generally speaking, is neuroanatomical modeling and thus individual cell morphology a necessary requirement to maintain a truthful connection between biological and simulated brain structures even with growing regions? Work done by Washington et al. [11] corroborates this view by detecting a strong influence of dendritic morphology on the functional behaviour of real CA3 pyramidal cells while maintaining similar electrophysiological resources (channels, receptors etc).

To approach this question in our network setting, we'd need to incorporate 72 individual pyramidal cells - a number not even available as reconstructed data in the famous Southampton Cell Archive. We therefore chose to follow the path to "produce" cell morphologies in computo and incorporate them, following single cell simulation, into our

Methods and Results

Analysis from reconstructed cells

A simple analysis tool, written in MATLAB, reads reconstructed morphologies from swc-files (www.cns.soton.ac.uk/~jchad/celArchive/cellArchive.html and www.koki.hu/~gulyas/) and provides growth parameters as described by [2]. We investigated 15 pyramidal cells and 15 interneurons including their variances:
the main and terminal dendrites cross sectional area ($S_{stem}/\mu m^2$; $S_{term}/\mu m^2$),
their respective lengths to the next branching point ($L_{norm}/\mu m$; $L_{term}/\mu m$),
the diameter ratios between daughters R(d/d);
the diameter ratio from mother to bigger daughter branch R(m/d);
the branching angle _ between two daugthers;
the branch taper _A ;
and the minimal mother branch area in _m.

Unfortunately, only one reconstruction of a Purkinje cell was found on the web, but nevertheless analyzed and used for in computo growth.
Pyramidal cell morphologies were split for their basal and apical dendrites and analysed separately.

Table 1:

Cell type	**S_{stem} /µm²**	**S_{term} /µm²**	**L_{norm} /µm**	**L_{term} /µm**
Pyramidal cells				
apical dendrites	2,64±1,41	0,14±0,02	34,64±39,18	111,73±50,12
Basal dendrites	0,59±0,79	0,05±0,01	31,84±26,21	125,72±46,18
cr				
Interneuron	0,56±0,27	0,07±0,03	116,08±130,96	134,72±96,5
Purkinje cell	25,79	0,89±0,05	10,1±7,27	7,69±8,57

Table 2:

Cell type	R (d/d)	Min	Max	R(m/d)	Branching angle _	Taper _A	Min mother in _m
Pyramidal cells							
apical dendrites	2,24±1,35	1	4,84	1,08±0,33	62.9±31,9	0,0006±0,066	0,005±0,06
Basal dendrites	1,09±0,26	1	1,98	1,11±0,32	66,14±34,22	0,004±0,05	0,068±0,01
cr							
Interneuron	1,3±0,61	1	2,8	1±0,11	73,67±30,44	0,003±0,13	0,13±0,15
Purkinje cell	1,28±0,43	1	3,94	1,14±0,25	79,60±31,14	0,09±0,21	0,26±0,13

Results, as listed in Table 1 and 2, corroborates data published by Hillman and others [1, 2,

Our Matlab program doesn't only analyse swc-files, but transfers them to and from GROGRA-compatible, GENESIS-compatible and VRML-conform file formats.

Neuroanatomical Modelling

In computo growth was performed using the extremely compact but powerful L-system type Growth Grammar Interpreter GROGRA freely available on www.uni-forst.gwdg.de/~wkurth/grogra.html. This program is originally designed to simulate and analyse the growth of real trees in a forrest (sensitive growth grammar) [3, 4], but is without a change able to model dendritic trees as well. See for example Purkinje cells in Figure 1. It takes variations of reported values into its growth process and provides this quite realistical views of dendritic trees (see Figure 3).

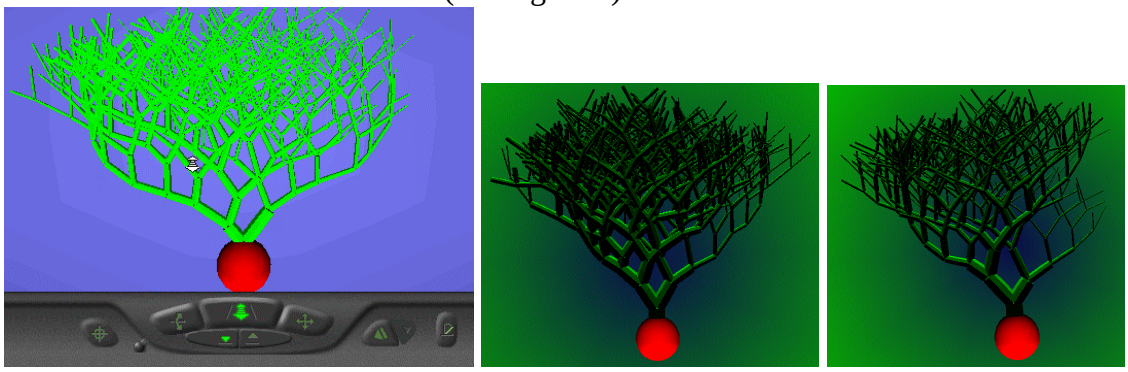

Figure 1: Examples of GROGRA modeled Purkijne cells, displayed in a VRML browser.

The only drawback of this powerful program, which even includes analysis and display tools, is its current focus on wooden trees, leading to a limited set of analysis routines. Thats why we wrote the Matlab routines mentioned above.

Compartmental simulation

We utilize the freely available neural simulator GENESIS to perform compartmental modelling with our synthetic morphologies. This part of this study is currently work under progress, but simulations running the University of Antwerps Purkinje Cell Tutorial with our synthetic morphologies show promising results (Figure 2). We transfer the resulting GROGRA files (.dtg) into a GENESIS morphology file and simulate functional single cell behaviour of different morphologies by mapping the same channel and receptor distribution to all cell under scrutiny.
Aim of this project is to replace the single cell morphology our small network by realistically grown morphologies and thus gaining even more realistic extracellular data [5].

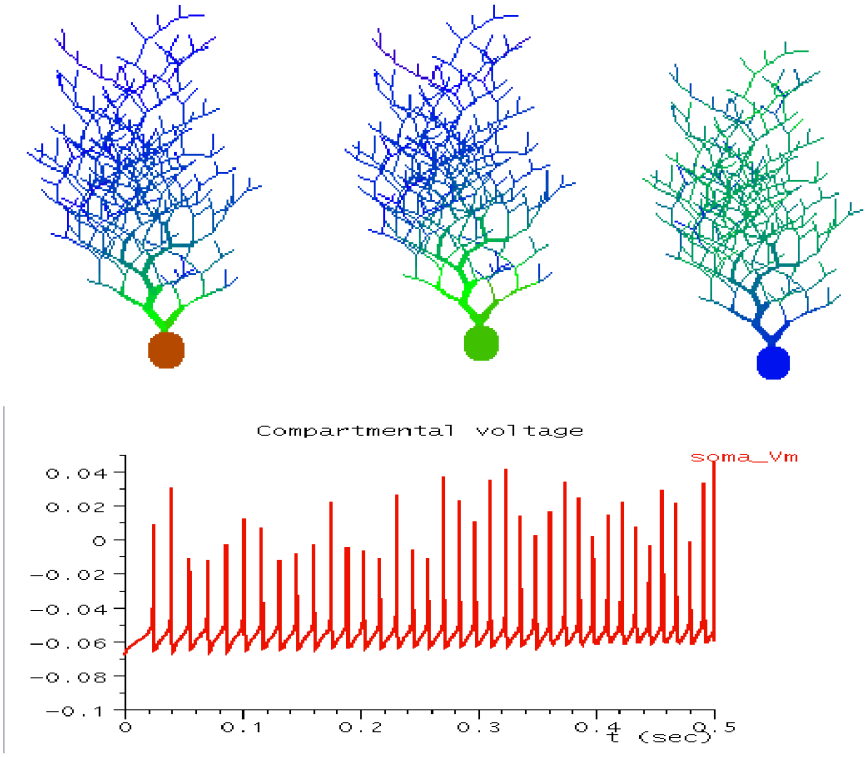

Figure 2: Example of a simulation with a synthetic purkinje cell morphology. Upper row from left to right: Potential initiation, propagation and dendritic follow-ups; Below: Plot of simulated somatic potential.

Display of Results

In order to make an inspection of synthetic dendritic trees more easy than done with GROGRAs own display system, we translated resulting morphologies into VRML-compatible files and display them in any available VRML-browser. (e.g. Cortona).

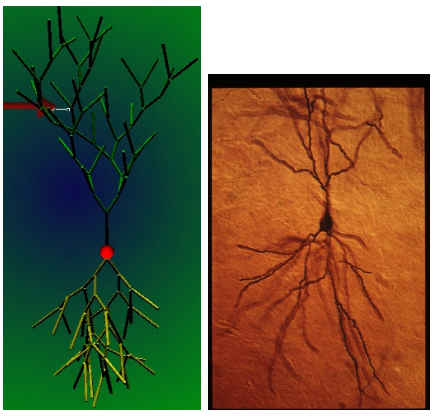

Figure 3: Example of a synthetic and a real Pyramidal cell. Real cell picture courtesy of O. Schmitt, Anatomical Institute, MU of Lübeck

This enables us to relay GENESIS compartmental simulation results to be used as color-coding descriptor for each VR-compartment, thus avoiding GENESIS' cumbersome display module while even facilitating a walk through the functional cells in question.

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