A proof-of-concept process for validated brain emulation boot-strapped on an in-silico fully known ground-truth neural circuit

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Abstract: (This will need to be re-written... the text here is temporary.) There is presently not a single published proof-of-concept example where a process of brain emulation has been carried out at some scale and where a validation was performed to quantify the degree to which an emulation satisfies necessary success criteria. Scientific motivation to make progress in brain emulation depends on having a touch-stone implementation and reference evaluation to quantitatively improve upon. The only way to evaluate claims of brain emulation is through the use of metrics that compare an emulation with an original system. Similarity metrics must measure similarity in ways that matter to the goal of whole brain emulation, i.e. that satisfy cognitive success criteria. E.g. spike train timing is not duplicated, but the probability of spiking is modulated sensibly and the evolution of system attractors is plausible. Similarity metrics are needed at multiple levels and while some can be used only with fully known ground-truth systems, others will carry over to whole brain systems. The principle of brain emulation depends on the ability to satisfy cognitive success criteria while replacing implementation details at some scale. In analog, potentially chaotic systems, scale separation is achieved through the application of operational constraints. E.g. rhythms (brain) or clock cycles (computer), neural population activity (brain) or parity bits (computer), action potentials (brain) or binary thresholds (computer). The application of constraints at consecutive levels limits the size of each black box in system identification.

Keywords: brain emulation; system identification; similarity metrics; in-silico

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Introduction

(Here: tiny paragraph about "brain emulation".)

(Here: a paragraph about how the process of model building for emulation is different than the typical computational neuroscience model building process.) field of neuroscience that is aimed at neural circuit function reconstruction in a way that extends beyond the requirements explored in systems

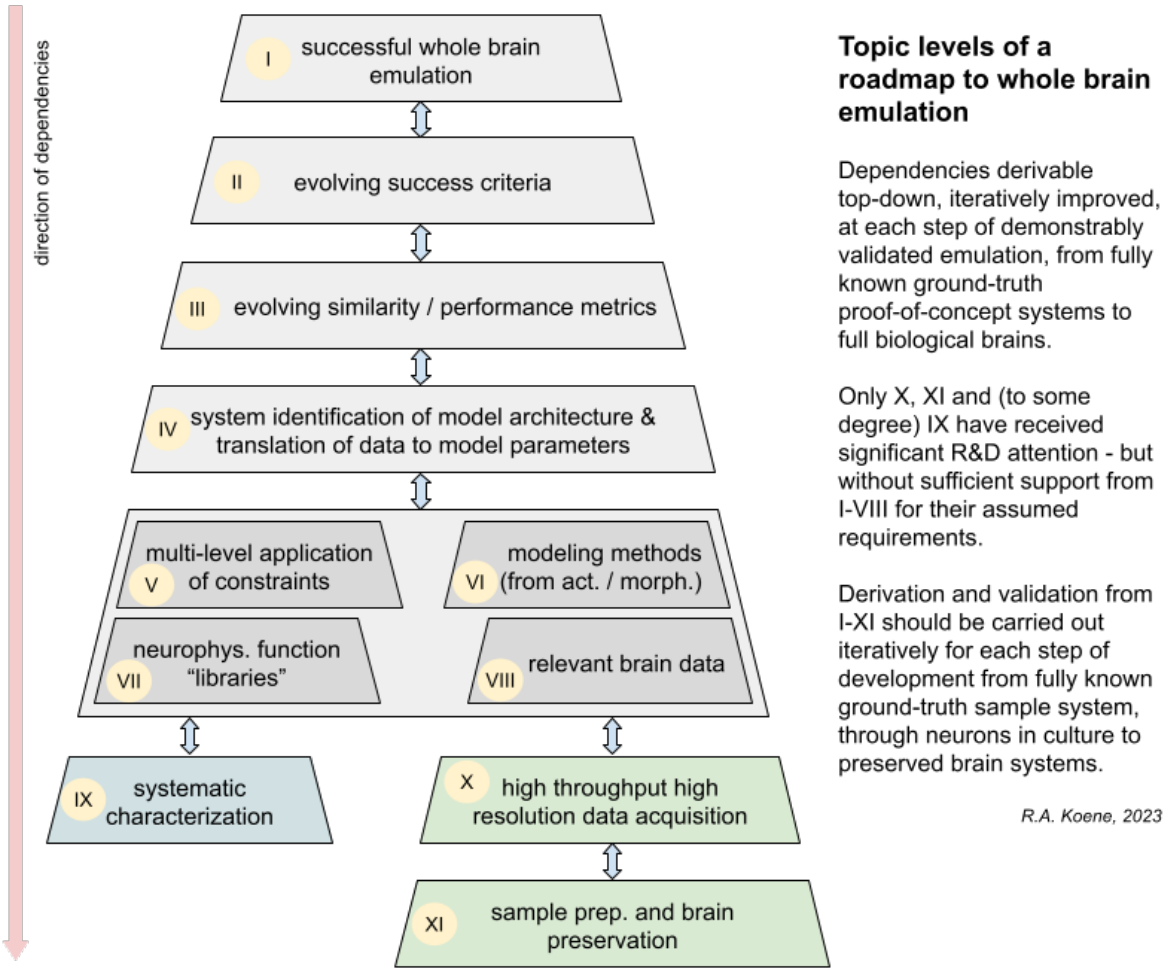

Figure 1. ***The dependencies pyramid from goals of successful whole brain emulation to brain data requirements.***

neuroscience, cognitive neuroscience, or neuroinformatics. Existing specializations have emphasized the use of computation for hypothesis testing in the context of fundamental but abstracted concepts. A neuroscience of reconstruction must emphasize not just shared operational fundamentals but individually unique functional structure, such as that which enables retrieval of personal memories.

(Here: Rewrite the sentences below into proper journal style and language.) There is presently not a single published proof-of-concept example where a process of brain emulation has been carried out at some scale and where a validation was performed to quantify the degree to which an emulation satisfies necessary success criteria. Scientific motivation to make progress in brain emulation depends on having a touch-stone implementation and reference evaluation to quantitatively improve upon. The only way to evaluate claims of brain emulation is through the use of metrics that compare an emulation with an original system. Similarity metrics must measure similarity in ways that matter to the goal of whole brain emulation, i.e. that satisfy cognitive success criteria. E.g. spike train timing is not duplicated, but the probability of spiking is modulated sensibly and the evolution of system attractors is plausible. Similarity metrics are needed at multiple levels and while some can be used only with fully known ground-truth systems, others will carry over to whole brain systems. The principle of brain emulation depends on the ability to satisfy cognitive success criteria while replacing implementation details at some scale. In analog, potentially chaotic systems, scale separation is achieved through the application of operational constraints. E.g. rhythms (brain) or clock cycles (computer), neural population activity (brain) or parity bits (computer), action potentials (brain) or binary thresholds (computer). The application of constraints at consecutive levels limits the size of each black box in system identification.

(Here: A paragraph that explains why the first example uses two imaginary ball-and-stick neurons.) The ball-and-stick example is intended to provide the simplest in-silico case with the smallest number of variables to address while still demonstrating the full process and dependencies chain for whole brain emulation (see Fig. 1). This is an opportunity to anchor the development of useful similarity metrics for brain emulation.

(Here: Describe the I-XI requirements in the pyramid figure. Remove the topic levels text from the figure and put that description in here instead.)

(Here: Explain that this example is worked out in explicit parts from I to XI as an opportunity to describe the process.)

Known ground-truth: In-silico sample preparation (XI) and characterized physiology (IX and VII)

(Here: A paragraph explaining how we equate characterized ephys and biological brain samples with VBP architecture and components.)

Table 1. ***The caption of an example table.***

Age Group	Training Group	Mean	SD
Children	Experimental Group	55.81	23.05
	Control Group	35.25	22.28
Adults	Experimental Group	67.45	15.84
	Control Group	40.41	15.04

Requirement IX: Establishing a set of virtual physiological components with well-characterized dynamics

(Here: Describe how the VBP is used to set up a "world" in which certain types of physiological components, our ball-and-stick neurons, exist that have been characterized to provide a modeling library.)

(Here: Mention how one would proceed on to the next more sophisticated step and towards working with real brain tissue for which there is no known ground-truth.)

Requirement VII: In-silico representation of virtual brain components

(Here: Describe preparation and use of the components library. Add reference to SW.)

Requirement XI: Preparation of the virtual brain architecture of the known ground-truth system

(Here: Describe how the architecture is set up. Add reference to SW.)

A virtual brain ground-truth system provides a "God's eye" record

(Here: Describe how every calculated variable can be recorded for analysis and how that aids the development of similarity validation metrics.)

(Here: Make it clear that this is not the same as experimental data acquisition from the origin system.)

Data acquisition: Double-blind experimentation in a virtual brain laboratory (X and VIII)

(Here: Describe that even though the ground-truth model is fully known to the designer, the experimenter is blind to this and can use only data obtained through in-silico data acquisition that mirrors the process of data acquisition from biological brain systems.)

Requirement X: In-silico experimental data acquisition

(Here: Describe the data acquisition set up with the previously prepared KGT system and running data acquisition simulations. Add reference to SW.)

Requirement VIII: Collected data and post-processing

(Here: Describe what it means for the collected data to be the "relevant" brain data.)

(Here: Describe the format of data obtained and how it may be post-processed for this simple experiment. Add reference to SW.)

System Identification and Translation to emulation model parameters (IV-VI)

(Here: Explain what system identification is, model selection and structuring. Explain what Translation means, model fitting. Point out the importance of constraints and their application. Explain that this

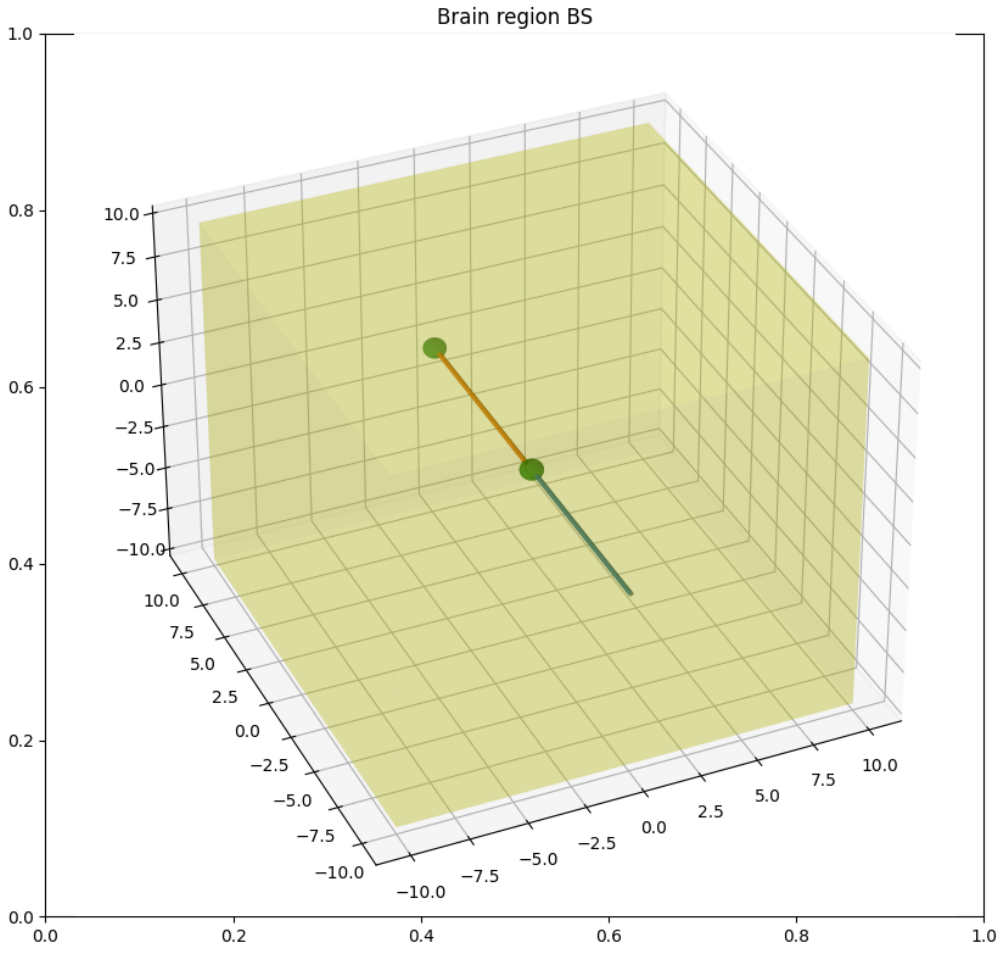

Figure 2. ***Diagram of the known ground-truth ball-and-stick neural circuit architecture within in-silico brain region.***

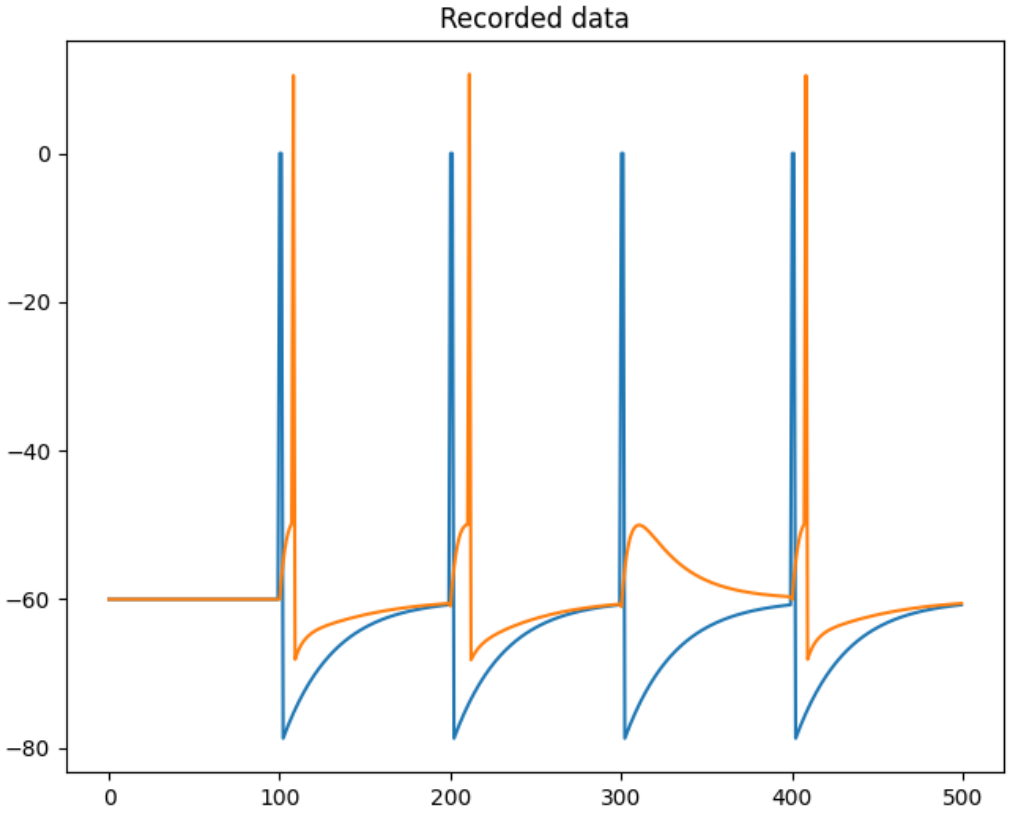

Figure 3. ***Plot of ball-and-stick neuron membrane potentials as recorded in "God's eye" mode during an experiment run.***

process can involve multiple concurrent attempts or repeated attempts, guided by the validation step and error identification.)

Requirement VI: Model selection and structure derivation from activity data and morphological data (VI)

(Here: Describe the process. Add reference to SW.)

Requirement V: Application of constraints at multiple levels (V)

(Here: Describe the process. Add reference to SW.)

Requirement IV: Completing a process of system identification and translation for model architecture and parameters

(Here: Describe the process. Add reference to SW.)

Validation of candidate emulated systems using similarity and performance metrics based on success criteria for successful whole brain emulation (I-III)

(Here: Describe similarity metrics that can be used in known ground-truth system and those that can be used in a broader category of systems, even biological brains. Explain that these will evolve as research proceeds from these most basic in-silico systems to more sophisticated systems.)

Requirement III: Measuring similarity and performance

(Here: Describe the application of metrics and the evaluation of results.)

Using known ground-truth systems to develop methods for the identification of error sources and their correction

(Here: Describe an example of an error and how its cause is determined. Describe how the system identification and translation is adjusted and the outcome improved. Add reference to SW.)

Requirement II: Meeting success criteria

(Here: Describe this important relationship.)

Requirement I: Achieving a successful whole brain emulation for the ball-and-stick neural system

(Here: Describe the outcome.)

Discussion

(Here: Discuss the main takeaways and important insights about the process for this simple system.)

(Here: Point to the follow-up research and the general procedure of step-wise advancement. Add a reference to the project and company.)

References

Kramer, W. (2019). Why i agree with the reference formatting guidelines set out by a.n. other. *Journal of Formatting Requirements, 4*(1), 301–303.

Other, A. (2019). References should have the standard blank line in between them, which means there is no need for a hanging indent. *Journal of Formatting Requirements, 3*(6), 125–129.

Phillips, N. D. (2018). Yarrr! the pirate's guide to r. *APS Observer, 30*.

Data, Code and Materials Availability Statement

(Here: Add links and DOIs to data, code and related materials.)

Authorship and Contributorship Statement

(Here: List who conceived the study, who designed the study and wrote the first draft of the manuscript. List other contributions. Mention if someone analysed data and revised the manuscript.)

All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgements

(Here: Add acknowledgments if applicable. This can include an acknowledgment of early support provided to the project.)

Appendices etc.

(Here: Only if applicable.)