TITLE: Analytical evaluation of expected values and variances of the targeting performances for a simplified neural growth model

AUTHORS: Adil Virani, Jun Xia, Gloria Sanin.

FACULTY SPONSOR: Remus Osan, Ph.D., Assistant Professor, Department of Mathematics and Statistics

Introduction: Spinal cord injury can lead to permanent damage of the ascending and descending neural pathways, which can perpetuate a loss of sensory feeling and motor control in the limbs. Consequently, post-traumatic treatment could consist of re- growing damaged axons to reestablish the pathways affected by the injury; however, this represents a challenge due to the following reason. During development chemical cues guide the growing neurons, thus helping them to reach the correct locations. Once this phase ends, these cues are not present anymore. This indicates that inducing additional neural growth can potentially lead to experimental therapies, but the issue of targeting the exact regions remains problematic. In this project, we evaluate the search efficiency of targets by neurons with stochastic arborization during developmental growth.

Method: We use a simplified stochastic model for the neural evolution. Initially, the tree starts with a single evolving neurite. This neurite can either branch and create two new active neurites that evolve on their own, with probability p, or it can continue advancing as a single active branch, with probability $q = 1 - p$. This process is repeated for each active neurite, creating probabilistic trees that range from very sparse to very dense. We restrict the possible trees by imposing a maximum total length L that cannot be exceeded. We then seed to compute the number of branches as a function of distance, which is reflective of the probability of success, using the probability table of all possible trees. Here we assume that the branches angles are small and that the branches evolve linearly in space. In addition to computing these expected values, we also seed to determine also the variances associated with the targeting success.

Results: We derive analytical results for the expected number of active branches close to the starting points. We also determine the associated variance as a series of polynomials in branching probability p. Finally, we numerically determine the global probability distribution function (pdf) for families of trees with values of maximum length L and probability p. The location of the maximum for pdf is the spatial location where this family of trees achieves maximum targeting performances.

Conclusion: Our findings are very informative about the expected performances that results from full-fledged numerical simulation of stochastically growing neurons. Despite the simplifications used, we anticipate that the these analytical results about the probability distribution will allow us to characterize the trends induced by variations in the parameters L and p in the numerical simulations. In turn, this will suggest how to use chemical agents that stimulate neural growth in order to fine-tune the optimal targeting region so that it coincides with the intended biological regions, thus reconnecting the neural pathways from brain to limbs.