Modeling and Analysis of Rhythmic Activities in Excitatory Networks of the Brain Stem and Spinal Cord

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The mechanisms underlying neural oscillations in the brain stem (e.g. in the pre-Bötzinger Complex, pre-BötC) and spinal cord that persist after inhibition blockade remain poorly understood. In this study, we use computer simulation and mathematical tools of bifurcation analysis and slow-fast decomposition to comparatively investigate several models of single neurons and excitatory neural populations incorporating different combinations of the intrinsic cellular mechanisms that may potentially operate in the pre-BötC and/or spinal cord. The persistent sodium current (I_{NaP}) and the Ca^{2+}-activated, cation nonspecific current (I_{CAN}) have been found in these regions and each can play a critical role in rhythm generation. I_{CAN} is believed to operate via intracellular Ca^{2+} oscillations and depends on intracellular Ca^{2+} from extracellular (Ca^{2+} currents) and/or intracellular (IP_3-dependent) sources. Our models incorporate I_{NaP}-dependent bursting, IP_3-dependent calcium oscillations and synaptically activated IP_3-production. Our analysis and computer simulations demonstrate the existence of several qualitatively different oscillatory regimes depending on single neuron parameters, external drive, and network interactions. The possible relevance of these oscillations to rhythmic activities in the pre-BötC and spinal cord in vitro is discussed. *Supported by NIH (R01 NS057815, R01 NS069220).*