Abstract

In this work the problem of epileptic seizure generation, progression and termination is addressed from a computational perspective. Two computational models are introduced, discussed and analyzed, aimed to reproduce the experimental data recorded in the entorhinal cortex of the *in vitro* guinea pig brain. This preparation is considered to be a valid reference model of human focal epilepsy. The goal is to shed light into the pathological mechanisms responsible for the occurrence, evolution and cessation of focal epileptic seizures. In particular, the traditional view according to which epilepsy is caused by a chain reaction of synaptic excitation is challenged. Alternative hypotheses of epileptogenesis are presented and tested by means of computer simulations. Emphasis is put on the role of non-synaptic mechanisms (i.e., mechanisms independent of synaptic transmission) and intra- and extracellular concentration dynamics of K^+, Na^+, Ca^{2+}, and Cl^- ions. Simulations results confirm the experimentally driven supposition that inhibition prevails on excitation at the outbreak of epileptic episodes, and prove that ion concentration changes shape the different phases of a focal seizure. A novel antiepileptic therapy is also investigated, presenting a potentially feasible strategy leading to successful seizure control.

Lawrence Gentletti