BMC Neuroscience

Poster presentation

Simulation of cytoskeleton influence on spatial Ca²⁺ dynamics in neuroendocrine cells

Amparo Gil*[1], Virginia González-Vélez[2], Javier Segura[3], Cristina J Torregrosa-Hetland[4], José Villanueva[4], Inmaculada López[4] and Luis M Gutiérrez[4]

Address: [1]Depto. Matemática Aplicada y C. Computación, Universidad de Cantabria,39005-Santander, Spain, [2]Area de Química Aplicada, Universidad Autónoma Metropolitana-Azcapotzalco,02200-México D.F., México, [3]Depto. Matemáticas, Estadística y Computación, Universidad de Cantabria, 39005-Santander, Spain and [4]Insto. de Neurociencias, Universidad Miguel Hernández-CSIC, Sant Joan d'Alacant, 03550-Alicante, Spain

Email: Amparo Gil* - amparo.gil@unican.es

* Corresponding author

This abstract is available from: http://www.biomedcentral.com/1471-2202/10/S1/P31

Introduction

The adrenal medulla inside the adrenal glands, which is situated over the kidneys, is composed of chromaffin cells. These cells release vital hormones like epinephrine and norepinephrine in response to stress. Cell depolarization force calcium channel opening which allows external calcium to enter inside the cell; this in turn activates vesicles towards release. Once Ca²⁺ enters inside the cell, it is heterogeneously distributed in different zones of the cytoplasm and the F-actin cytoskeletal network seems to play a crucial role in this dynamic behavior [1]. Cytoskeleton is a dynamic supporting structure inside the cell that exhibits a very complex 3-D polygonal shape. It forms walls and empty spaces in the cytosol. In chromaffin cells, we have found that the highest levels of Ca²⁺ are found in the interior of cytoskeletal cages (empty spaces), whereas Ca²⁺ is low in the cytoskeletal walls. This possibly happens because this structure is acting as a physical barrier. Since cytoskeleton is not a static structure, its complex dynamics would affect the Ca²⁺ spatial distribution along time and finally, it would also has an impact on exocytosis. Moreover, we have also encountered evidences that calcium channels are organized in clusters, and that they are positioned in the border of cytoskeletal cages together with secretory vesicles. Then, active sites for secretion (where release occurs) may be placed near empty spaces of cytoskeletal cages probably to allow efficient exocytosis.

Modeling and results

In this work and as a first modeling approach to the influence of the complex cytoskeleton structure on the calcium signal, we have tested two geometrical configurations of three clusters of three calcium channels each inside a cytoskeleton cage, in order to analyze the influence of a physical barrier on the spatial Ca²⁺ distribution after the channels open. We have modeled a prototype cytoskeleton 3-D cage as a cylinder (radius = 0.3 µ per height = 1 µ) and then make a 3-D grid of small cubes of 30 nm per side. The cylinder boundaries represent the cytoskeleton, the physical barrier for Ca²⁺ diffusion. We have simulated the calcium influx in response to a short depolarizing pulse for two different arrangements of channel clusters. The first simulated configuration (A) corresponds to one in which clusters are located in the limits of a cytoskeleton cage, while in the second simulated configuration (B) the clusters are located in the centre of the cage. We have evaluated the 3-D calcium buffered diffusion using a microscopic Monte Carlo scheme [2]. For configuration A, we observe that the Ca²⁺ signal reaches higher values than Configuration B near the location of the clusters. This con-

figuration also induces a more heterogeneous spatial distribution of the calcium signal than the corresponding spatial distribution obtained for configuration B.

Conclusion

We have found that Ca^{2+} increases faster and higher when clusters of calcium channels are placed in the border of cytoskeletal cage, where secretory vesicles are also located. Therefore, our findings support the hypothesis that clusters might be positioned in the cytoskeleton limits in order to achieve a more efficient response of the secretory machinery.

References

1. Giner D, *et al.*: **Real-time dynamics of the F-actin cytoskeleton during secretion from chromaffin cells.** *J Cell Sci* 2005, **118:**2871-2880.
2. Gil A, *et al.*: **Monte Carlo simulation of 3-D buffered Ca diffusion in neuroendocrine cells.** *Biophys J* 2000, **78:**13-33.