Group 1-2

Localization of CaMKII within a Spine by Diffusion of Calmodulin

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Localization of Activated Ca^{2+}/calmodulin-Dependent Protein kinase II within a spine: Modeling and computer simulation

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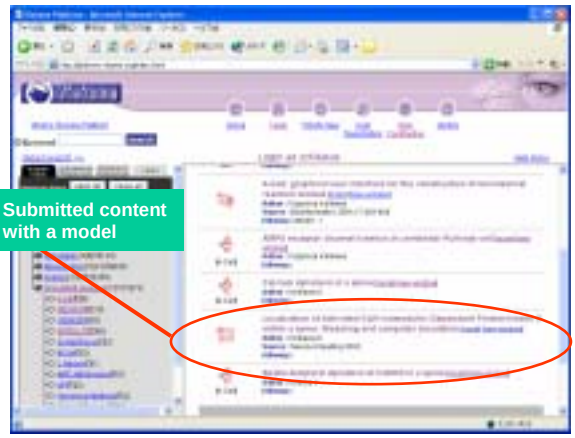

Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) plays a crucial role in the induction of long-term potentiation (LTP). One form of LTP expression is thought to be the phosphorylation of glutamate receptor channels by CaMKII. Thus the localization of activated CaMKII within a spine will affect the expression of LTP. The translocation of activated CaMKII to PSD was reported. Here we investigated the localization of activated CaMKII in a model dendritic spine, and found that the diffusion of calmodulin and calcineurin but not CaMKII contribute to the localization of activated CaMKII near PSD. This will offer an additional mechanism for the localization.

Summary

Localization and translocation of CaMKII are thought to be important for the induction of LTP and LTD. Here we investigated the localization of active CaMKII by simulations of a biochemical reaction model in a three-dimensional spine morphology. Unexpectedly, we found that the diffusion of calmodulin increased the degree of localization of active CaMKII near PSD in a spine.

Model

Present model was constructed by A-Cell and A-Cell-3D, which are free software downloadable from Visiome Platform.

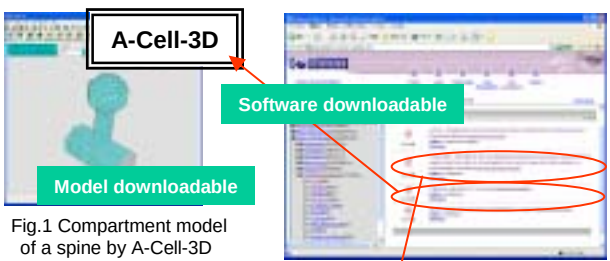

Fig.1 Compartment model of a spine by A-Cell-3D

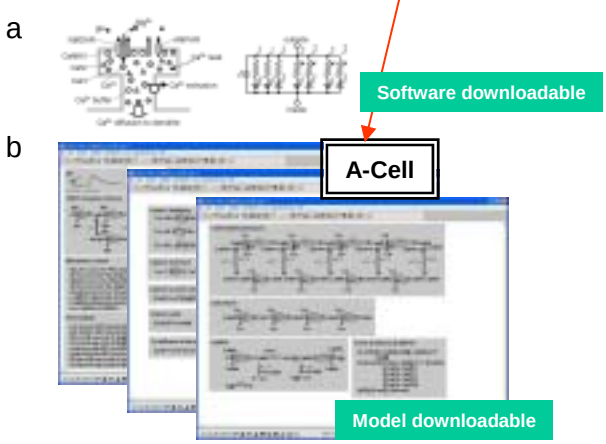

Fig.2 Biochemical reaction model using A-Cell

The biochemical reaction model includes 1) activation of AMPAR and NMDAR, 2) change in the membrane voltage, 3) Ca inward flow through NMDAR, 4) Ca buffering, 5) Ca leak and extrusion through membrane, 6) Ca diffusion, 7) activation of calmodulin (CaM), 8) activation of CaMKII, and 9) activation of calcineurin (CaN).

Results

Table 1 Simulations were performed under different combinations of diffusion for Ca, CaM, CaN, and CaMKII.

Exp. #	diffusion			
	Ca	CaM	CaN	CaMKII
Exp.1	Y	N	N	N
Exp.2	Y	Y	N	N
Exp.3	Y	Y	Y	N
Exp.4	Y	Y	Y	Y

Fig.3 Spatial distribution of active CaMKII. Diffusion of CaM increased the localization. In addition, diffusion of CaN confined active CaMKII almost near PSD.

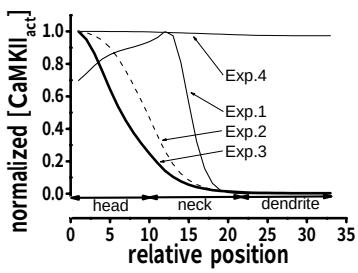

Fig.4 Spatial profile of active CaMKII

Conclusion

Unexpectedly, diffusion of CaM and CaN increased the degree of localization of active CaMKII within a spine head, thereby helping the translocation to PSD.

References

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Shen, K., et al, Sience, Vol.284(1999), pp.162-166.