

Release of L-Glutamate at the synapse

Gillespie, ME., Kavalali, E., Mahajan, SS.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://reactome.org/licenses/).

16/05/2024

Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 88

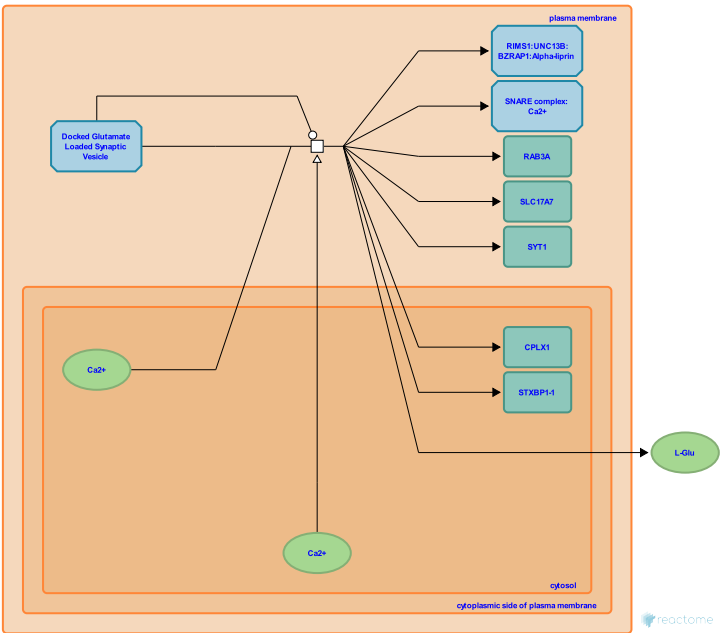
This document contains 1 reaction ([see Table of Contents](#))

Release of L-Glutamate at the synapse ↗

Stable identifier: R-HSA-210430

Type: transition

Compartments: extracellular region, plasma membrane, cytosol



Once vesicles are docked, primed and ready to be released fusion of the synaptic vesicle with the plasma membrane can be triggered by an influx of Ca^{2+} through the voltage gated Ca^{2+} channels (N, P/Q and R type). Ca^{2+} influx initiates a cascade of events in which the Ca^{2+} sensing protein, synaptotagmin-1 (sty-1) is central. Sty-1 promotes the membrane fusion between the synaptic vesicle and the plasma membrane by Ca^{2+} dependant induction of membrane curvature. Synaptotagmin competes with SNARE complex binding in a Ca^{2+} dependent manner thereby displacing complexin-1 and causing membrane curvature and fusion of the synaptic vesicle with the plasma membrane. The fusion is characterized by the formation of a trans SNARE complex in which SNAP 25, syntaxin and synaptobrevin along with VGLUT1, the glutamate transporter, synaptotagmin, and Rab3a either become a part of the plasma membrane or membrane delimited in the vesicular membrane. Vesicle fusion ultimately results in the release of the glutamate into the synaptic cleft.

Literature references

Fisher, RJ., Craig, TJ., Burgoyne, RD., Morgan, A., Evans, GJ., Ciufo, LF. et al. (2003). Phosphorylation of Munc18 by protein kinase C regulates the kinetics of exocytosis. *J Biol Chem*, 278, 10538-45. ↗

Martens, S., McMahon, HT., Kozlov, MM. (2007). How synaptotagmin promotes membrane fusion. *Science*, 316, 1205-8. ↗

Jahn, R., Radhakrishnan, A., Stein, A., Fasshauer, D., Riedel, D. (2007). Synaptotagmin activates membrane fusion through a Ca^{2+} -dependent trans interaction with phospholipids. *Nat Struct Mol Biol*, 14, 904-11. ↗

Editions

| | | |
|------------|----------|----------------|
| 2008-01-14 | Authored | Mahajan, SS. |
| 2008-04-24 | Reviewed | Kavalali, E. |
| 2009-11-19 | Edited | Gillespie, ME. |