

Chapter 9: Biochemical Mechanisms for Information Storage at the Cellular Level

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By J. David Sweatt, Ph.D.

Chapter 9: Dendritic Spine



Summary: Three Primary Issues Related to Mechanisms for E-LTP

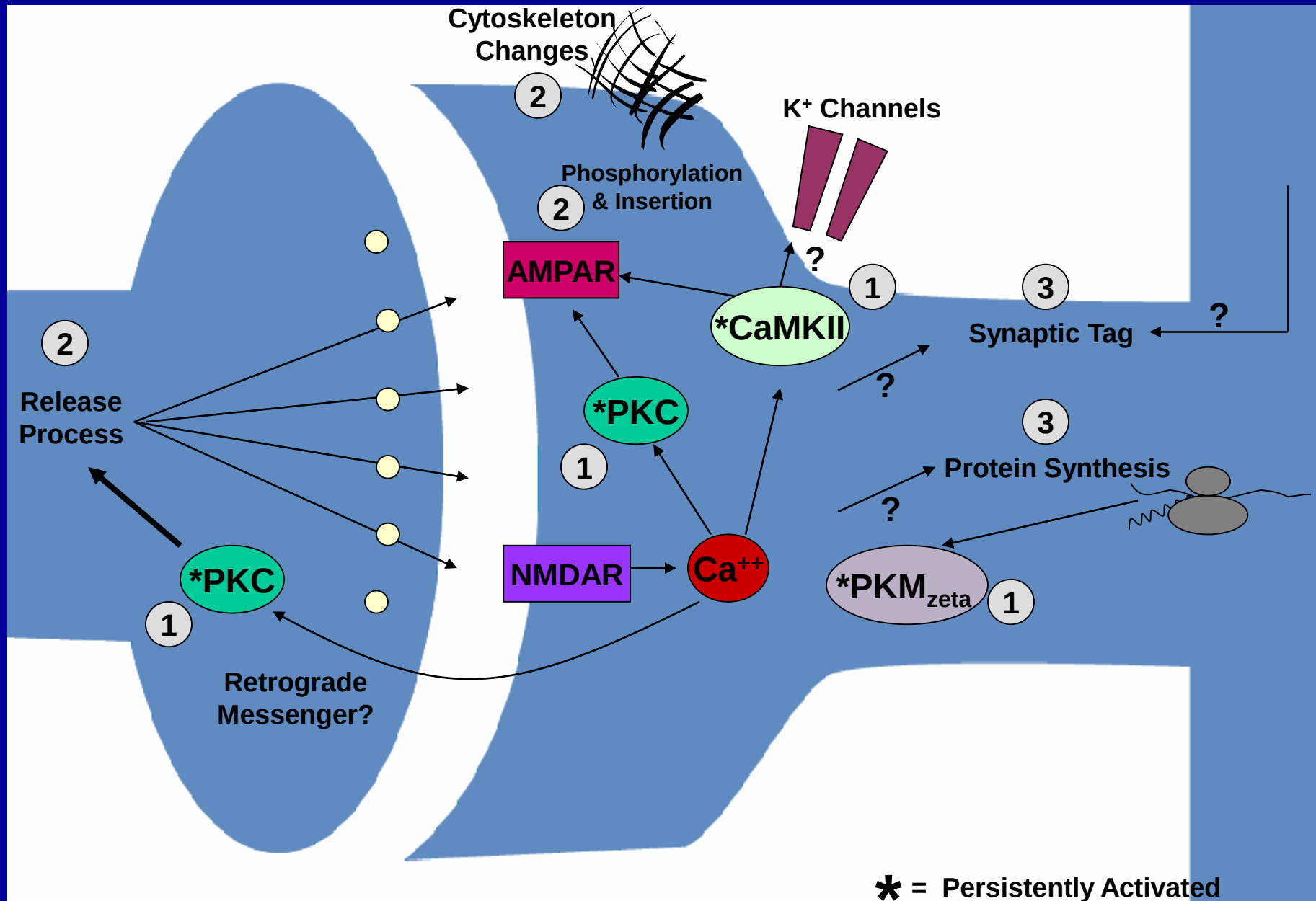


Figure 1

Structures of Calcium-Binding Proteins

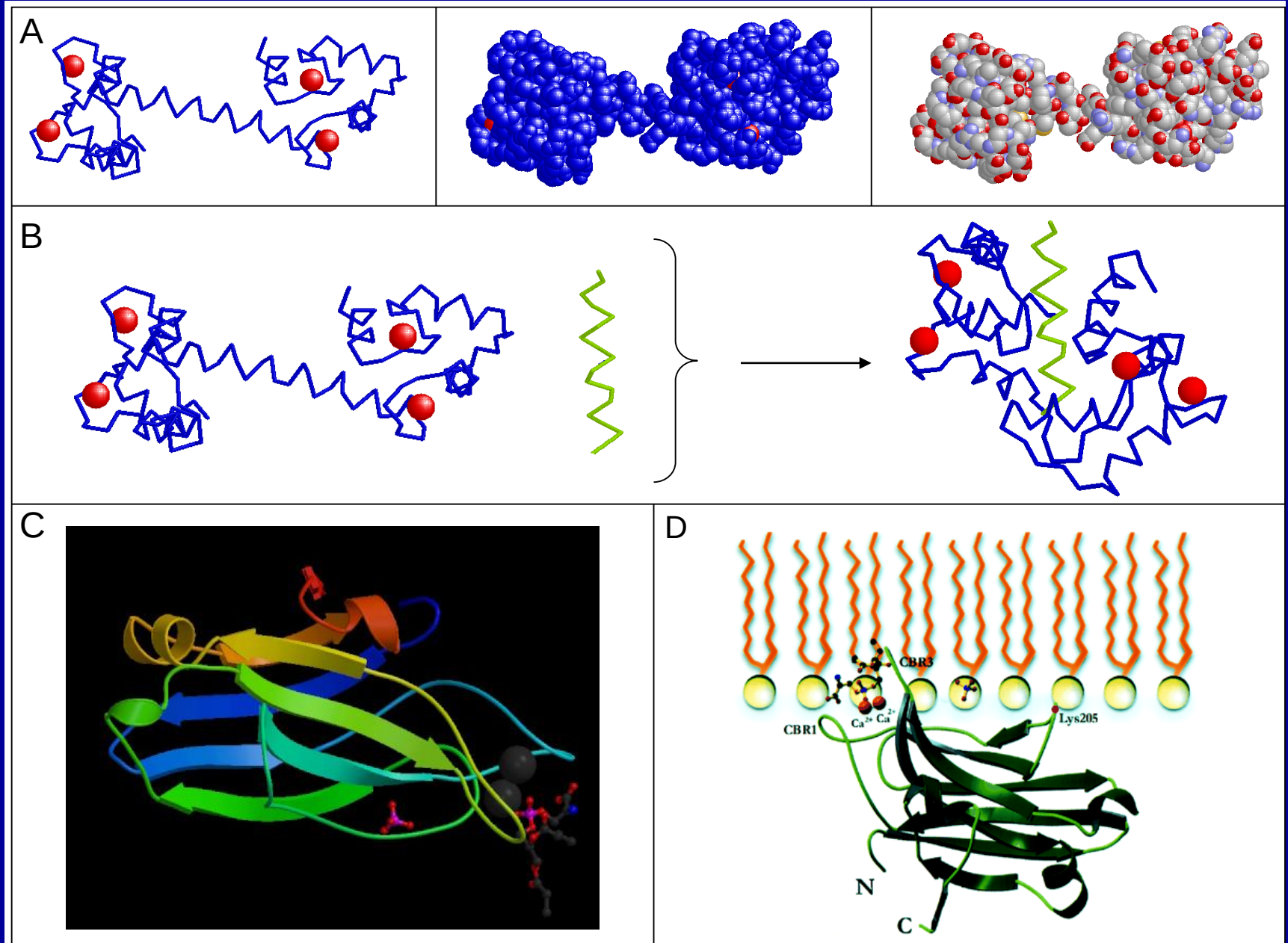


Figure 2

Structure of CAMKII

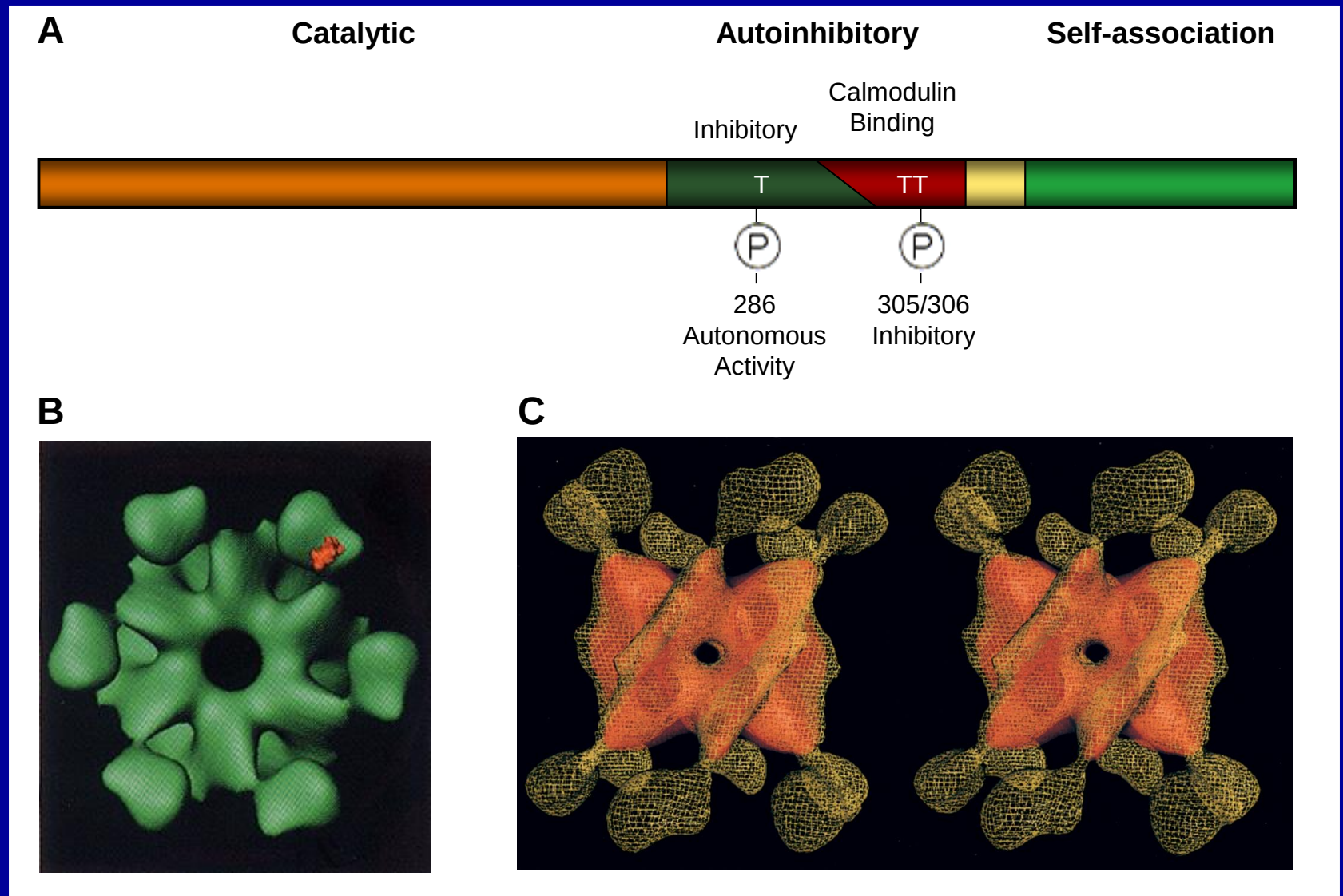


Figure 3

Three Different Effects of Ca/CaM on CaMKII

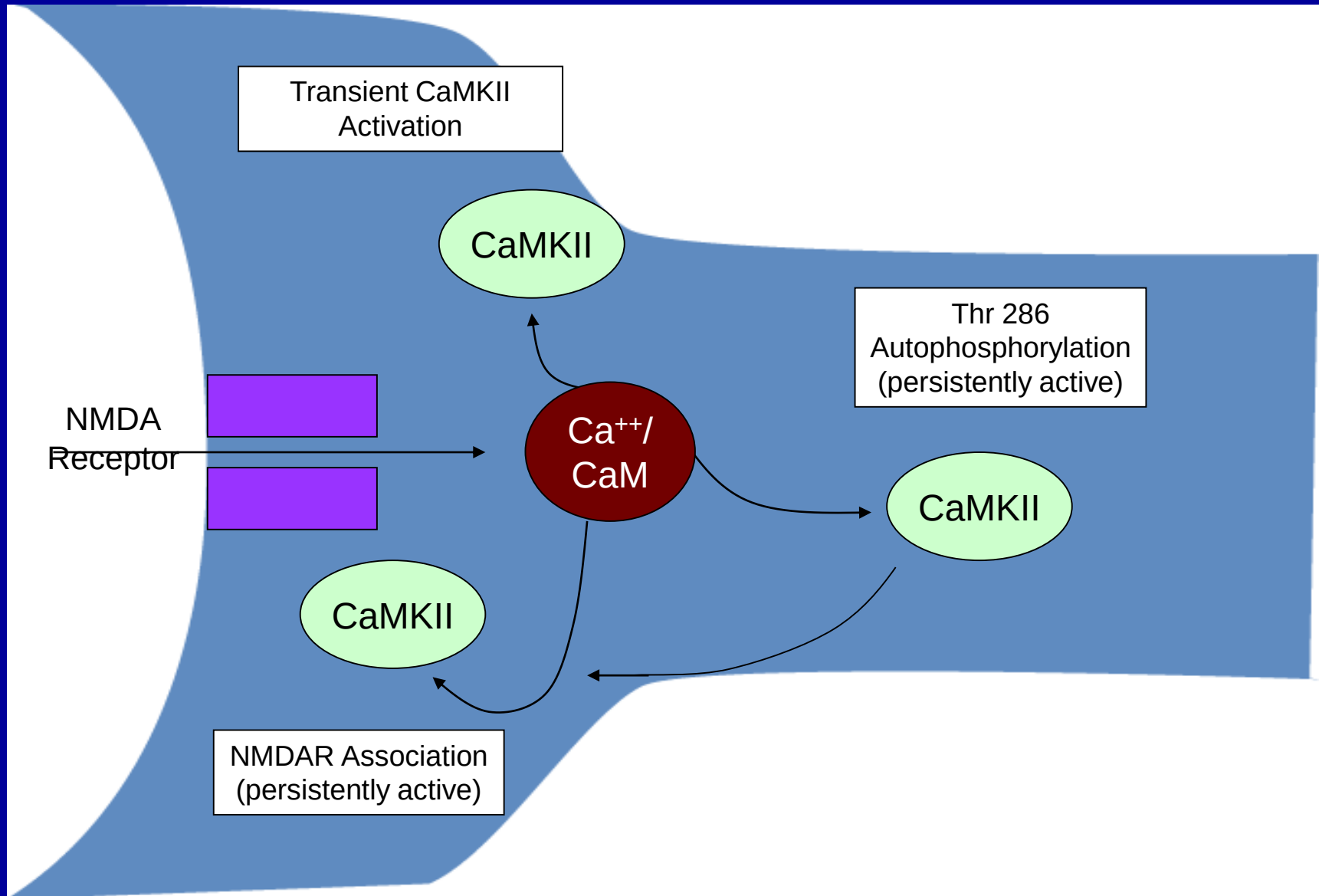


Figure 4

Catalysis of cAMP by Adenylyl Cyclases

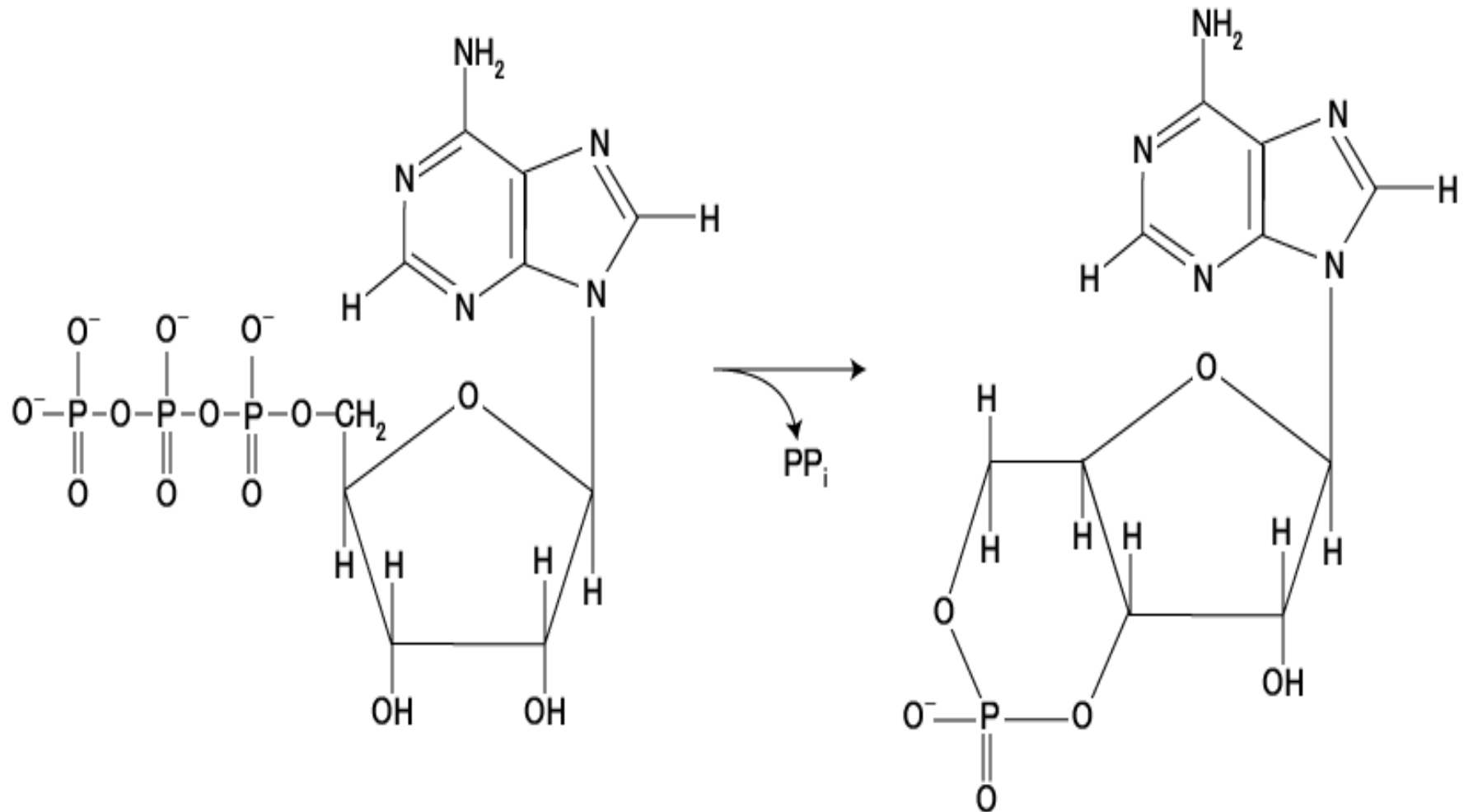


Figure 5

LTP in Adenylyl Cyclase-Deficient Mice

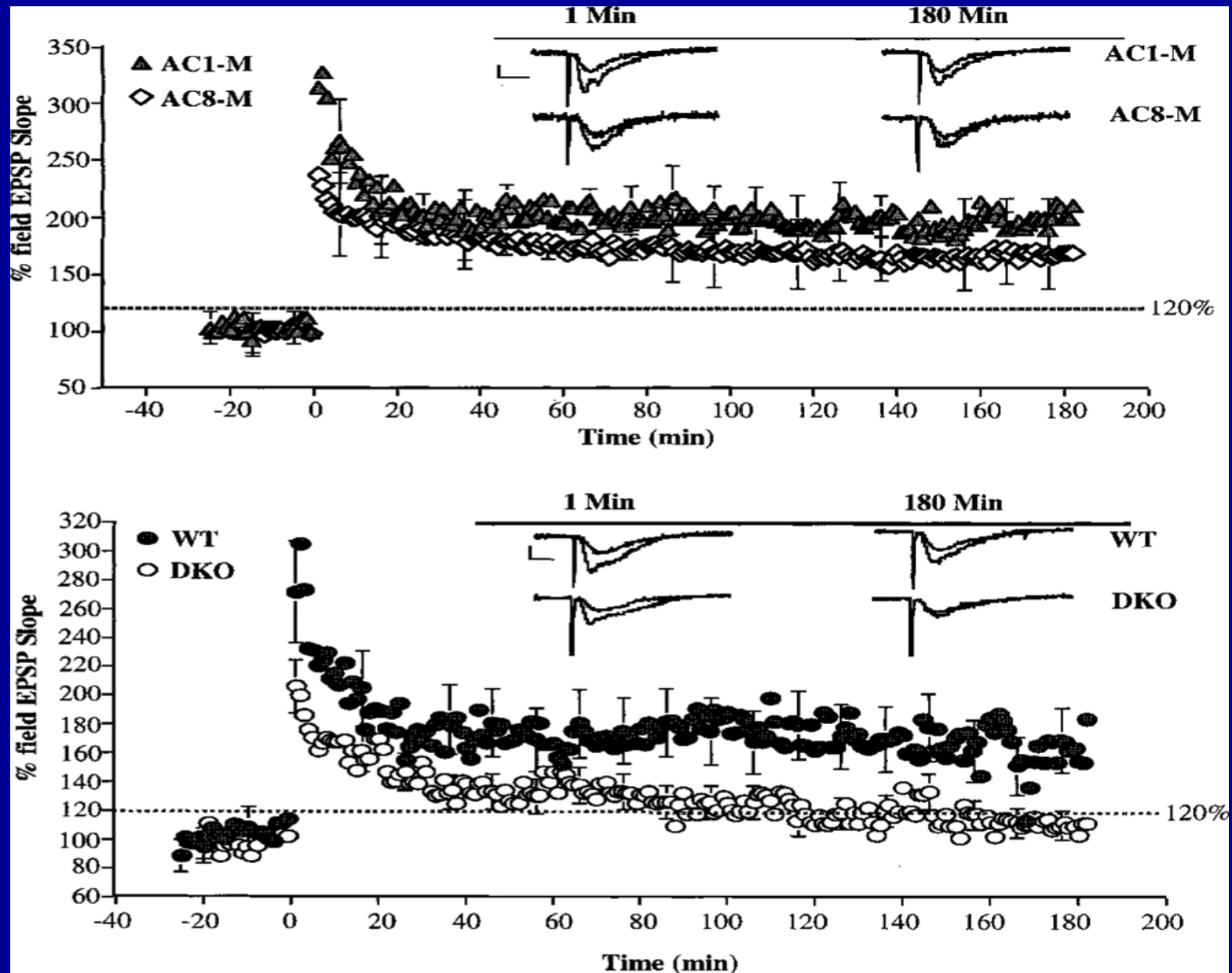


Figure 6

Domain Structures of Isoforms of PKC

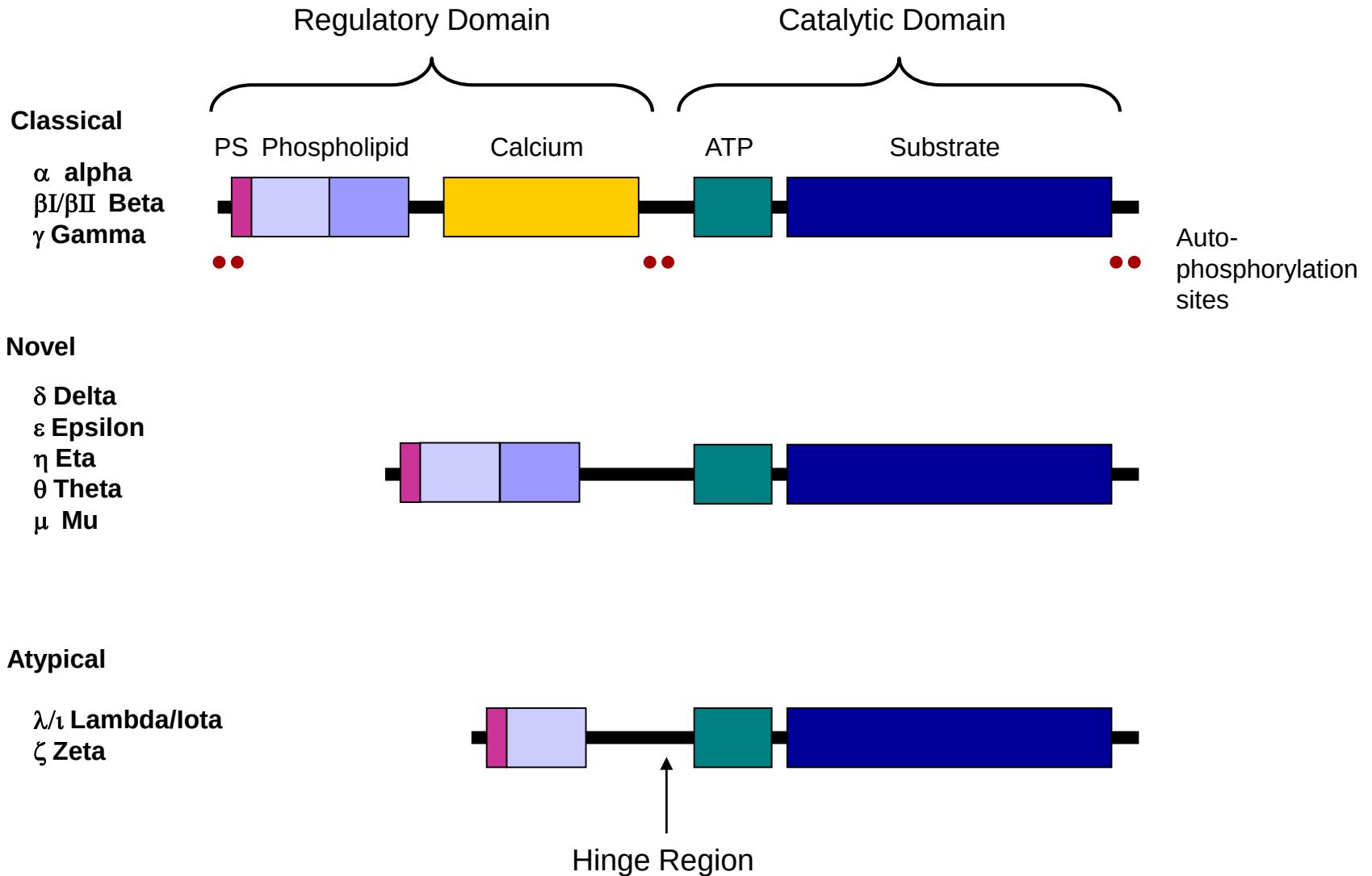


Figure 7

Hippocampal LTP in PKC Isoform-Specific Knockout Mice

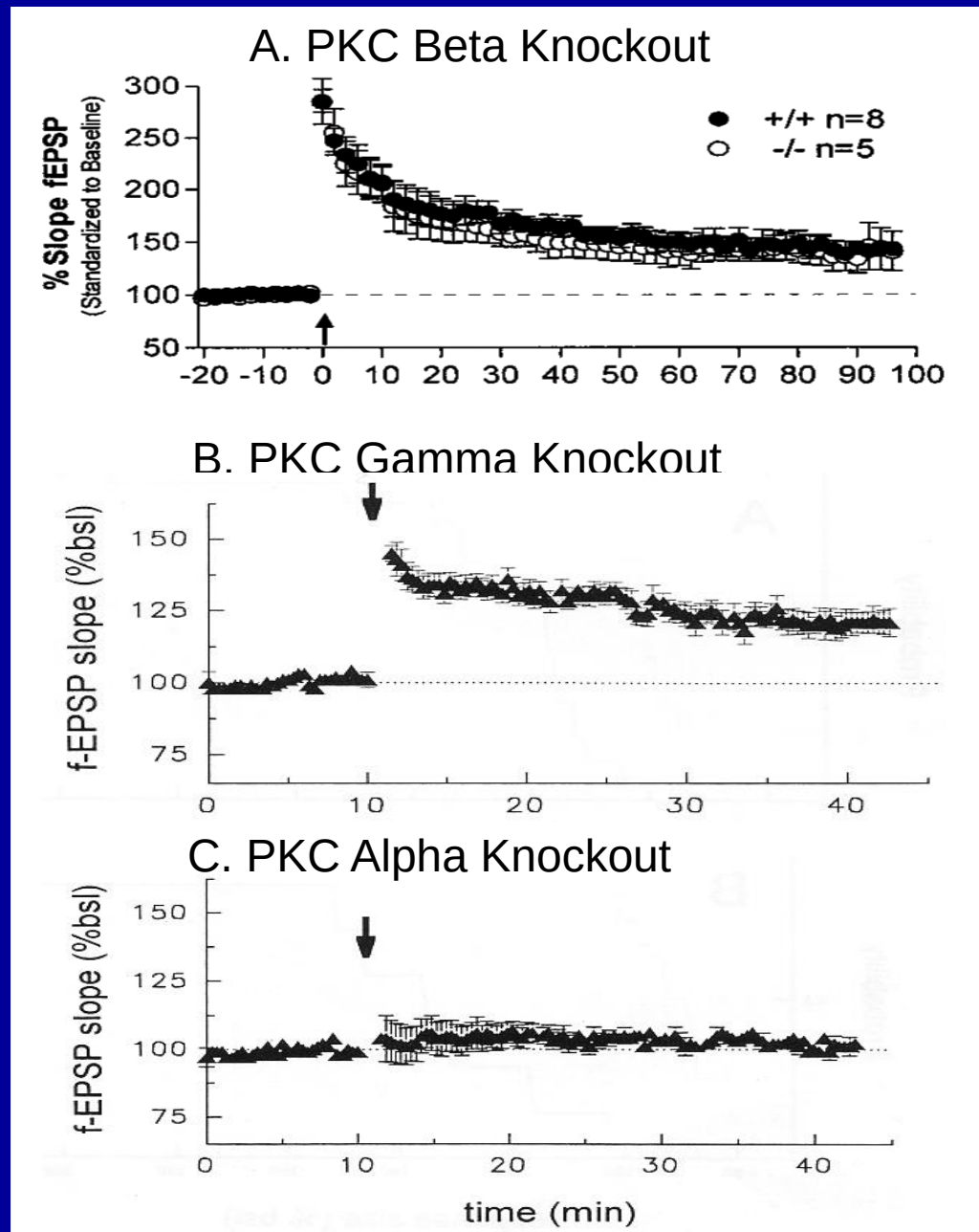


Figure 8

PKM ζ mRNA Formation from Internal Promoter within PKC ζ Gene

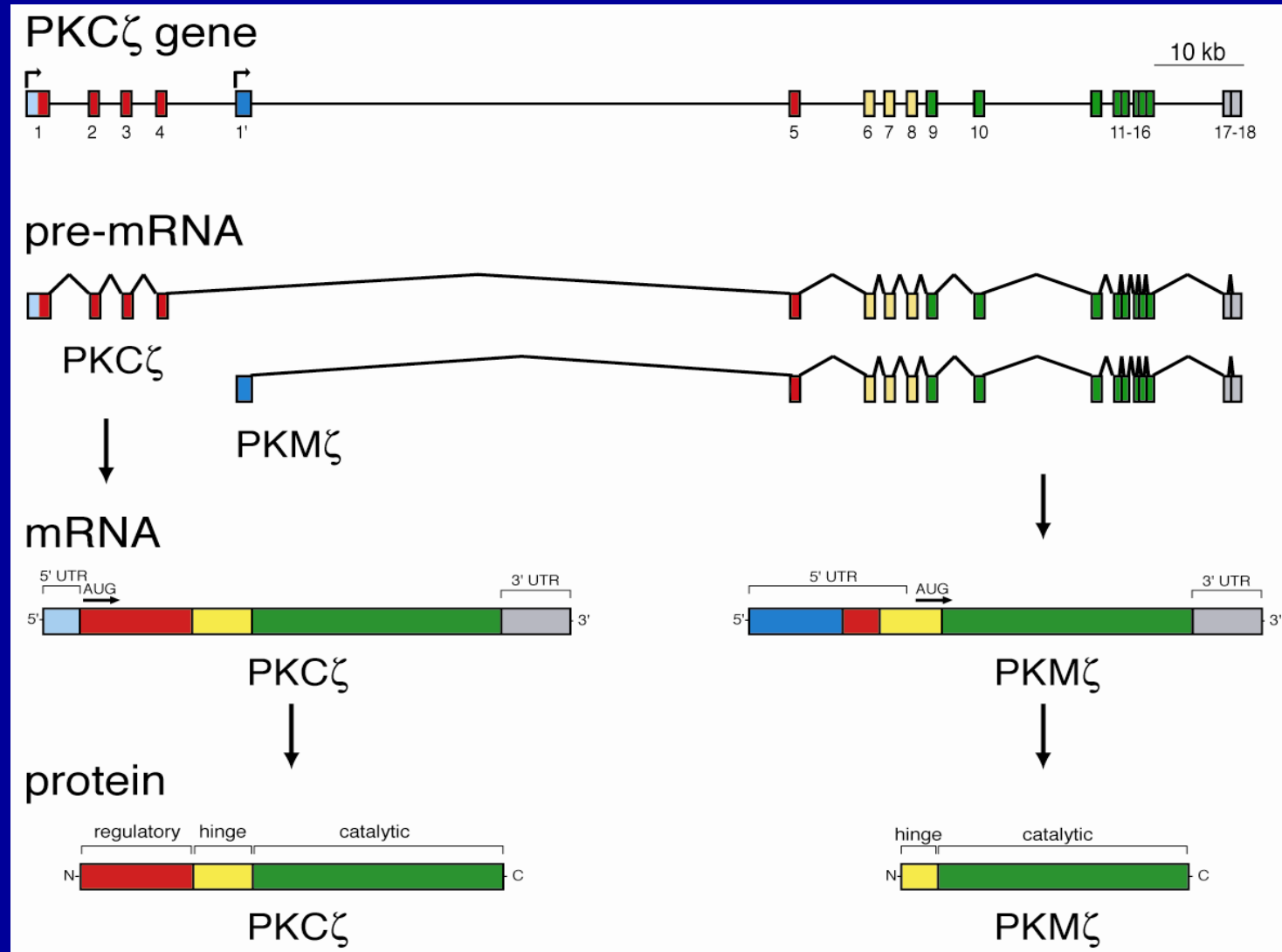


Figure 9

PKM ζ and LTP Maintenance

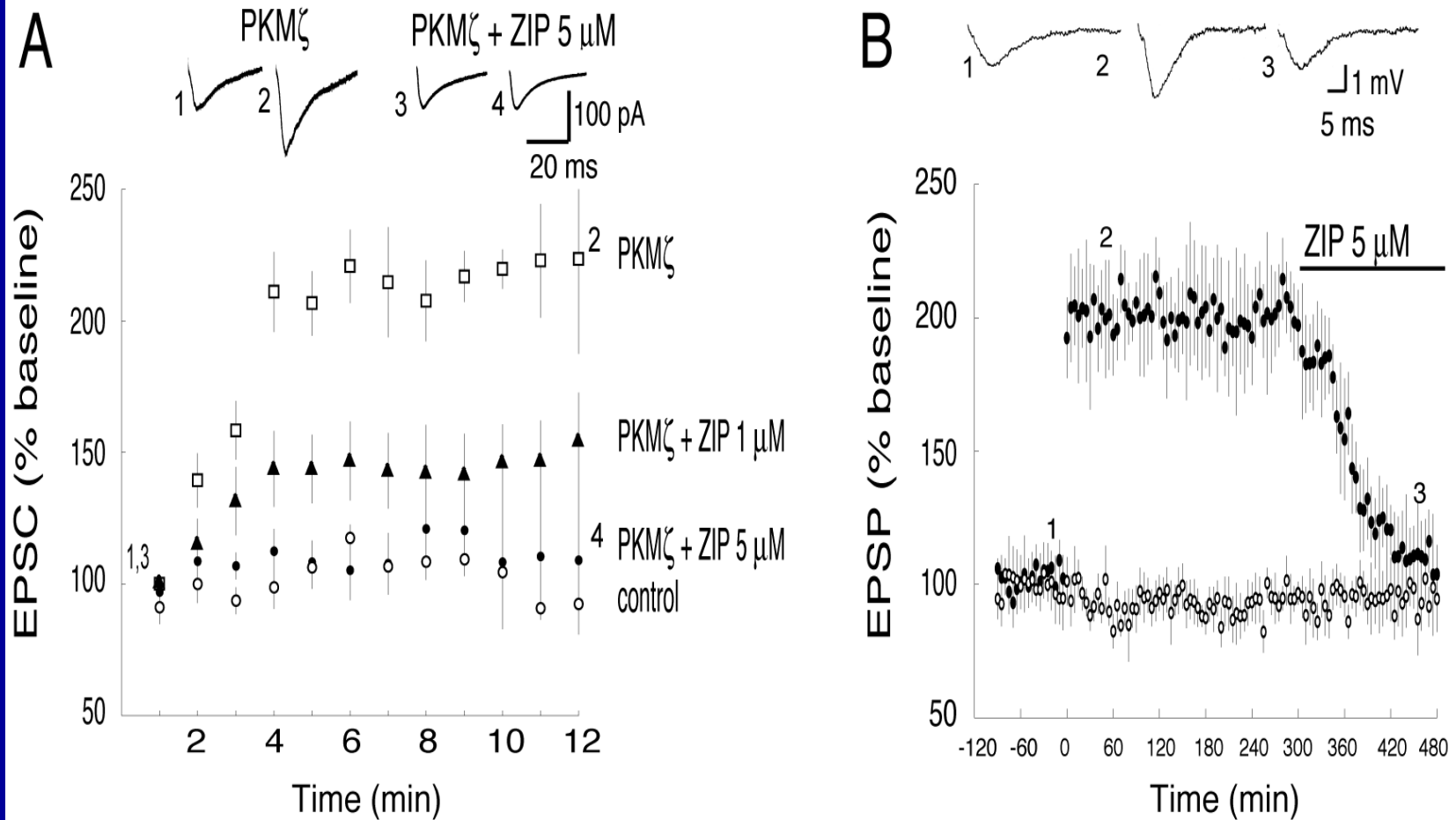


Figure 10

TABLE I: PROPOSED MECHANISMS FOR GENERATING PERSISTING SIGNALS IN E-LTP

MOLECULE	MECHANISM	ROLE
CaMKII	Self-perpetuating autophosphorylation	Effector phosphorylation,
	coupled with low phosphatase activity	Structural changes
Various PKCs	Direct, irreversible covalent modification by reactive oxygen species	Effector phosphorylation
PKM ζ	De novo synthesis of a constitutively active kinase	Effector phosphorylation

TABLE II: PROPOSED MECHANISMS FOR AUGMENTING AMPA RECEPTOR FUNCTION IN E-LTP

Mechanism	Likely molecular basis
Increased single-channel conductance	Direct phosphorylation of AMPA receptor alpha subunits by CaMKII or PKC
Increased steady-state levels of AMPA	CaMKII (+ PKC?) phosphorylation of AMPAR- associated trafficking and scaffolding proteins
Insertion of AMPAR into silent synapses	CaMKII phosphorylation of GluR1-associated trafficking proteins

AMPA Receptor Regulation During LTP

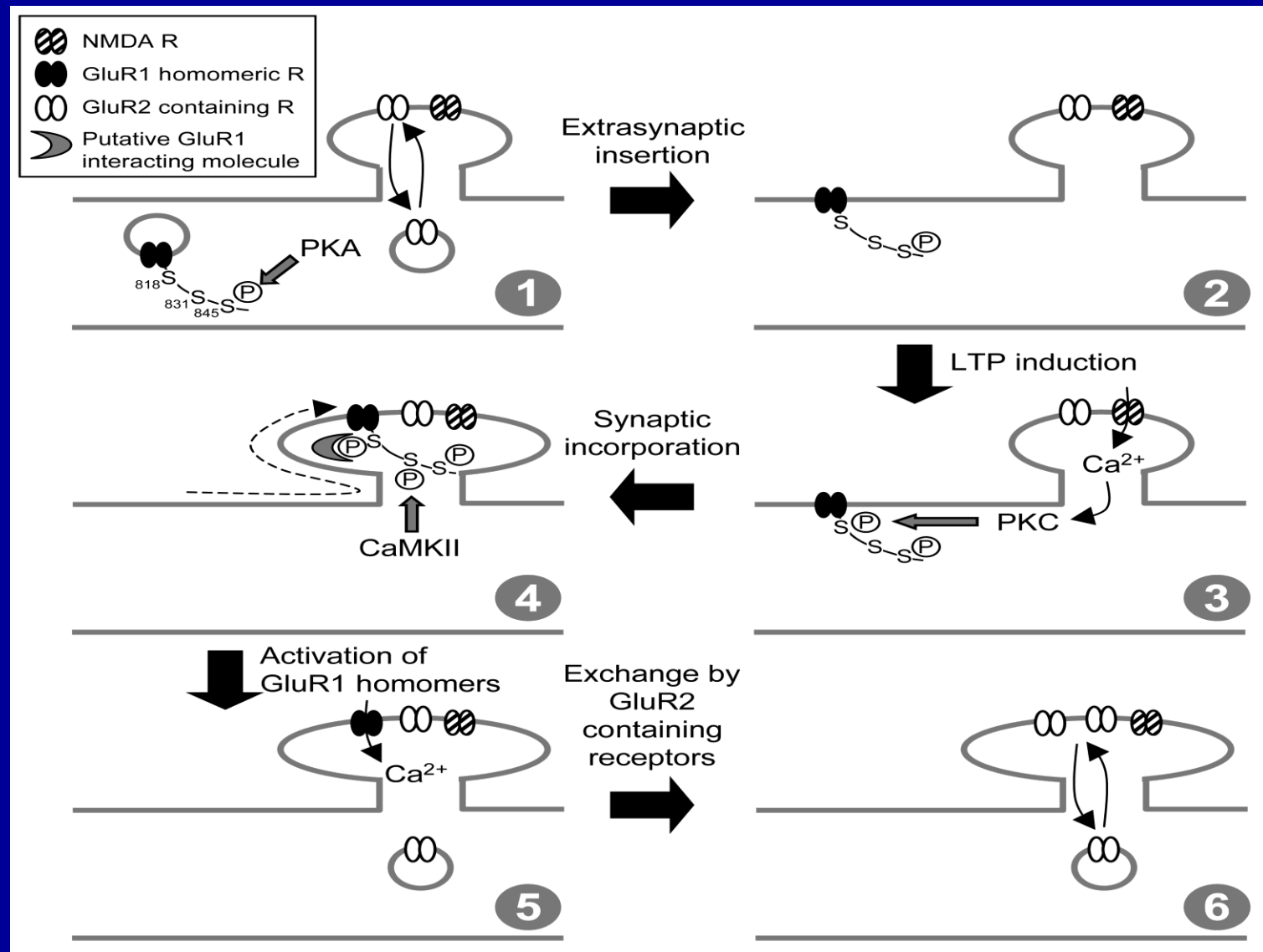


Figure 11

Glutamate Receptor Insertion and Stabilization in E-LTP

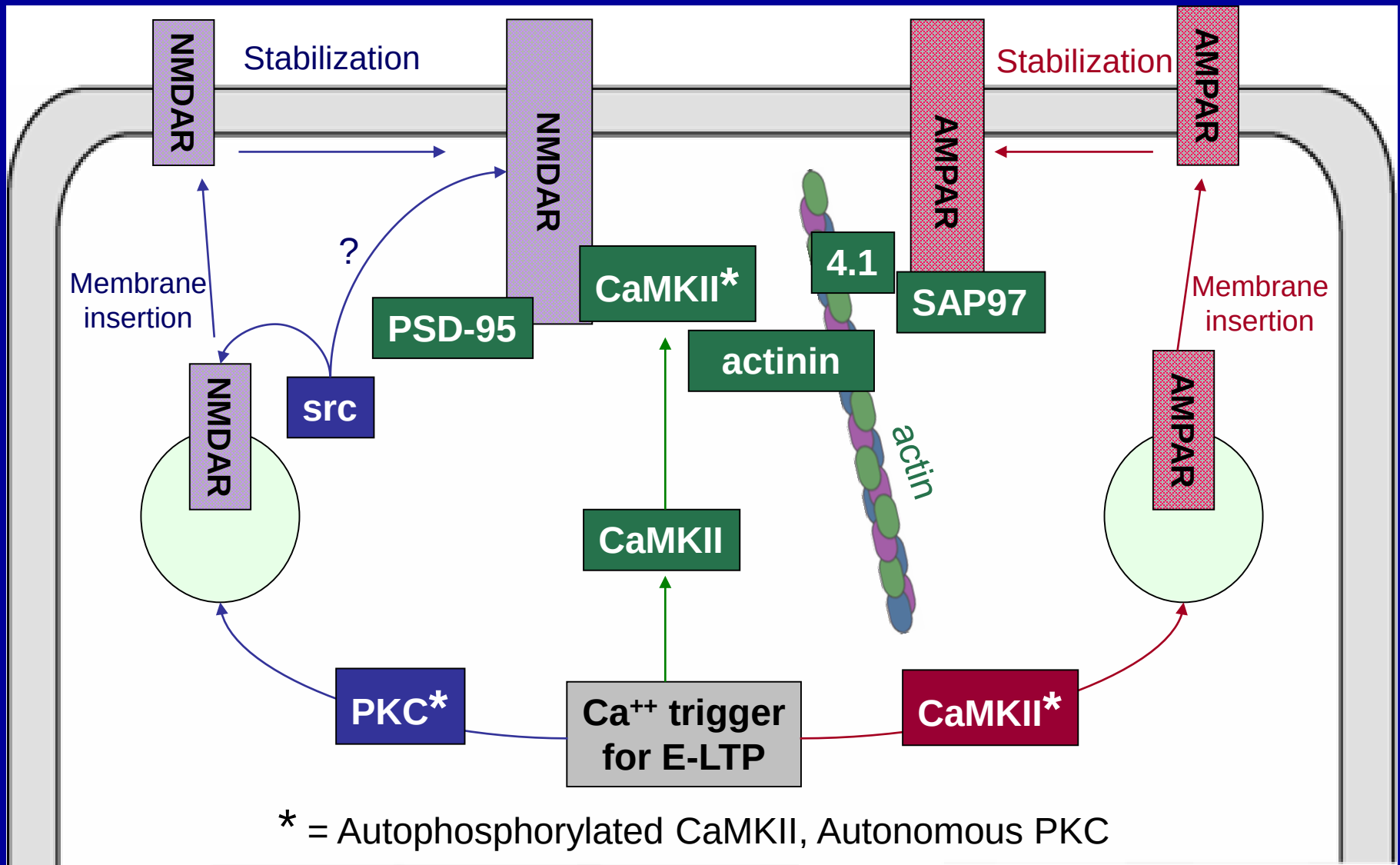


Figure 12

Retrograde Signaling in E-LTP

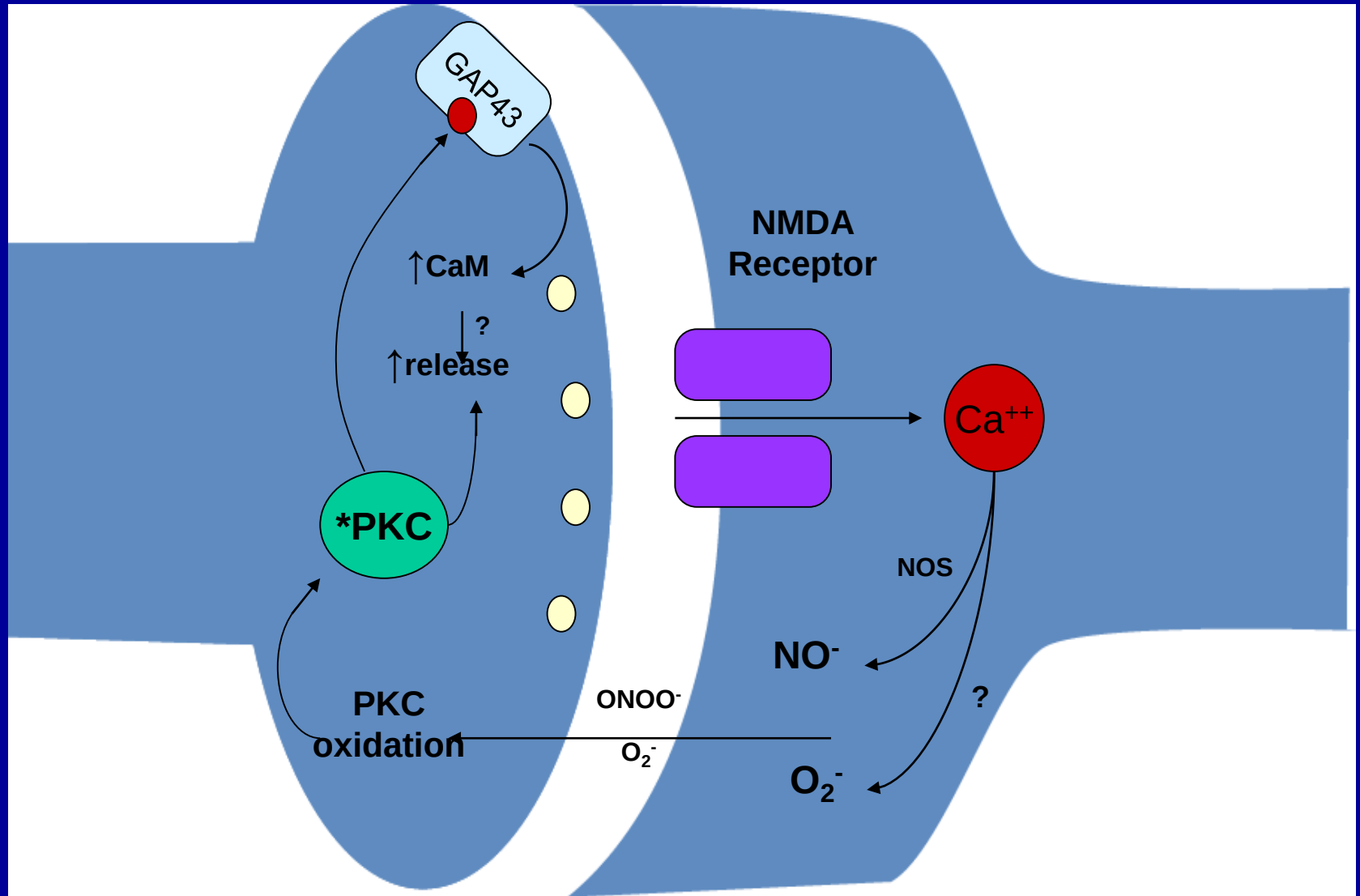


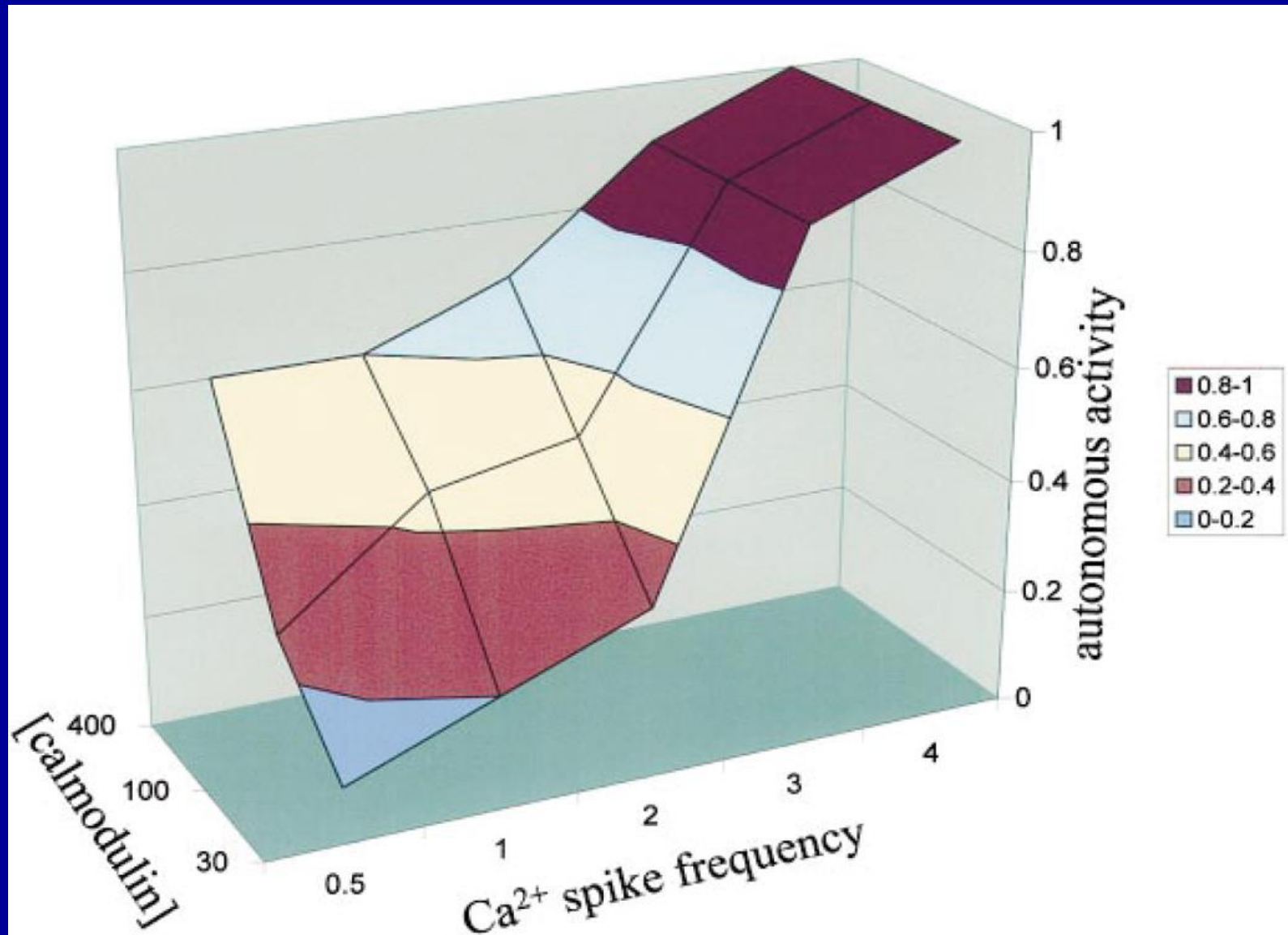
Figure 13

The diagram illustrates the signaling pathway for FMRP loss in FXMR. The NMDA Receptor and mGluR activate PKC, which in turn activates AKT and ERK. AKT activates mTOR, which activates RSK2. ERK activates mnk1, which activates eIF4E/eIF2B & other eIF's. RSK2 activates GSK3B. Both mTOR and GSK3B activate the Ribosomal S6 Protein. The Ribosomal S6 Protein is involved in Translation Initiation and Polyribosome complex formation. FMRP (lost in FXMR) is involved in mRNA Targeting. The Polyribosome complex leads to 1° & 2° alterations in dendritic protein synthesis, resulting in CaMKII?, PKM_{zeta}, PSD-95 associated proteins (SAPAP4), MAP1B (1° target of FMRP), and Arc. These changes lead to a Change in Spine Structure and Morphological Changes.

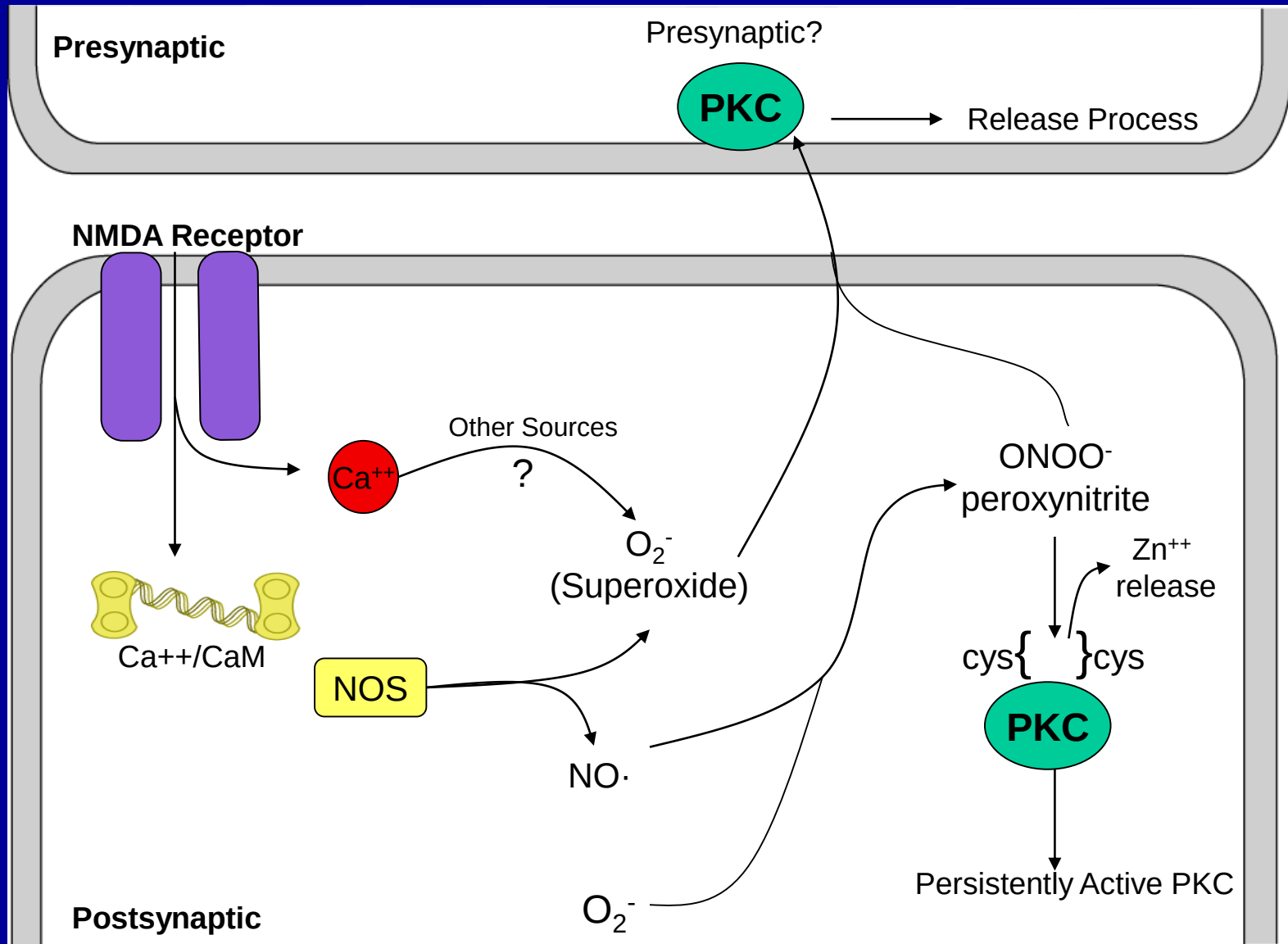
Figure 14

↓ Constitutive Protein Synthesis
↓ Induced Protein Synthesis

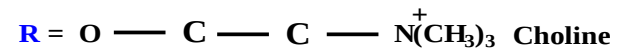
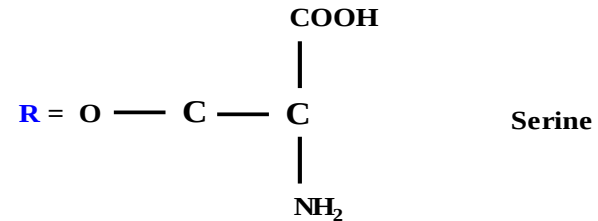
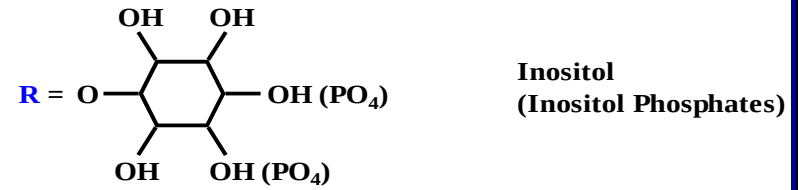
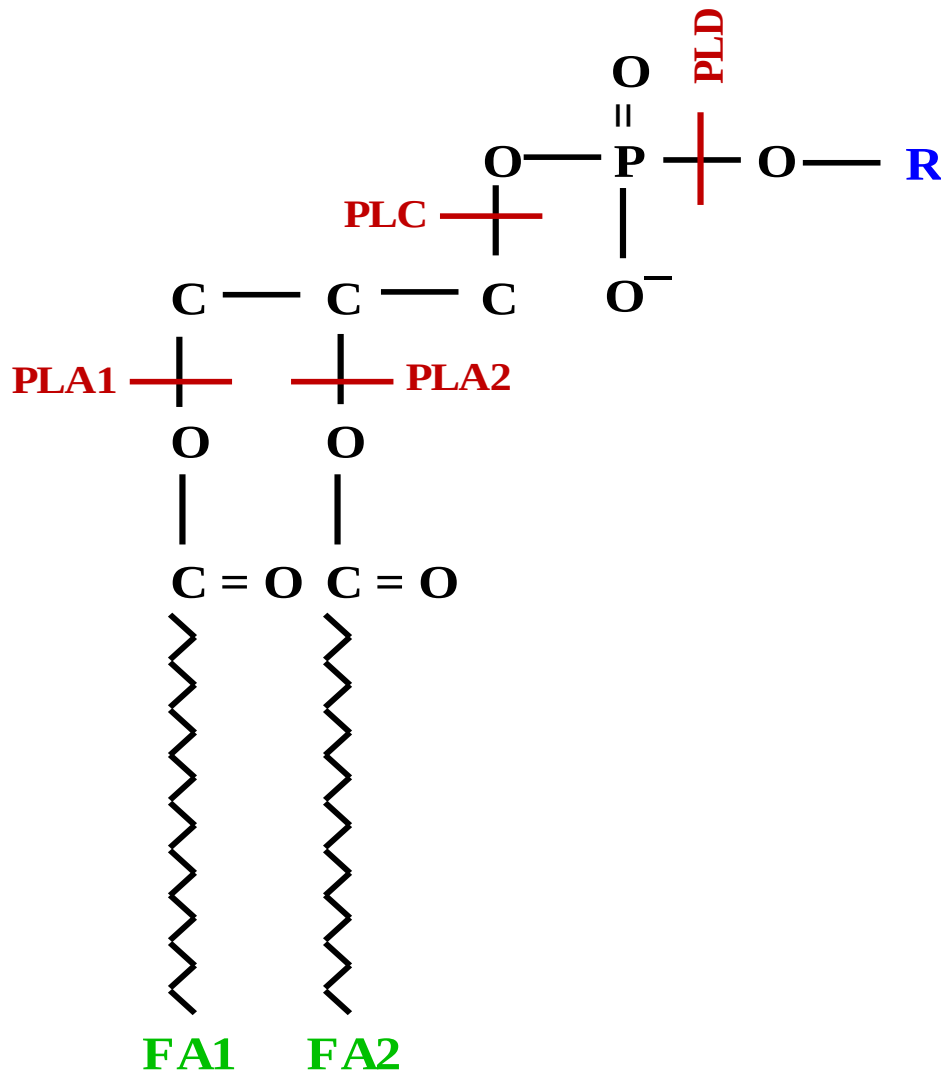
CAMKII as a Temporal Integrator



Oxidative Activation of PKC in LTP

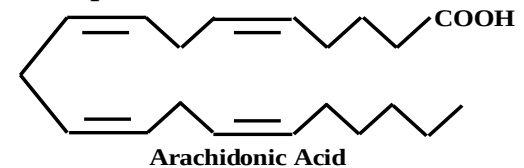


Sites of Cleavage of Phospholipids by Phospholipases



FA₁ = Any of a number of 16-20 carbon fatty acids

FA₂ = Typically Arachidonic Acid in plasma membrane



Synaptic Tagging and the E-LTP/ L-LTP Transition

