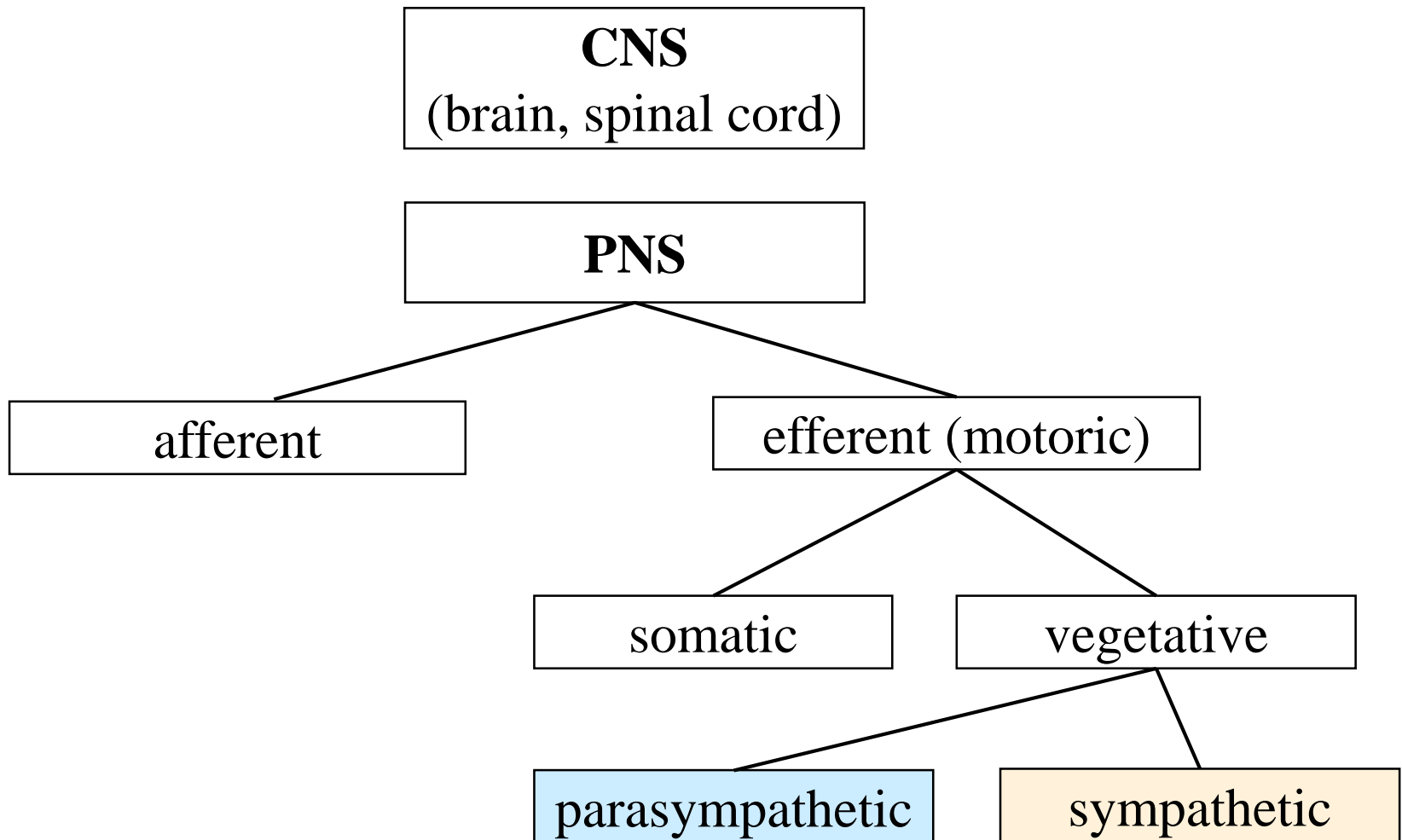


# **Signal transduction in vegetative nervous system**

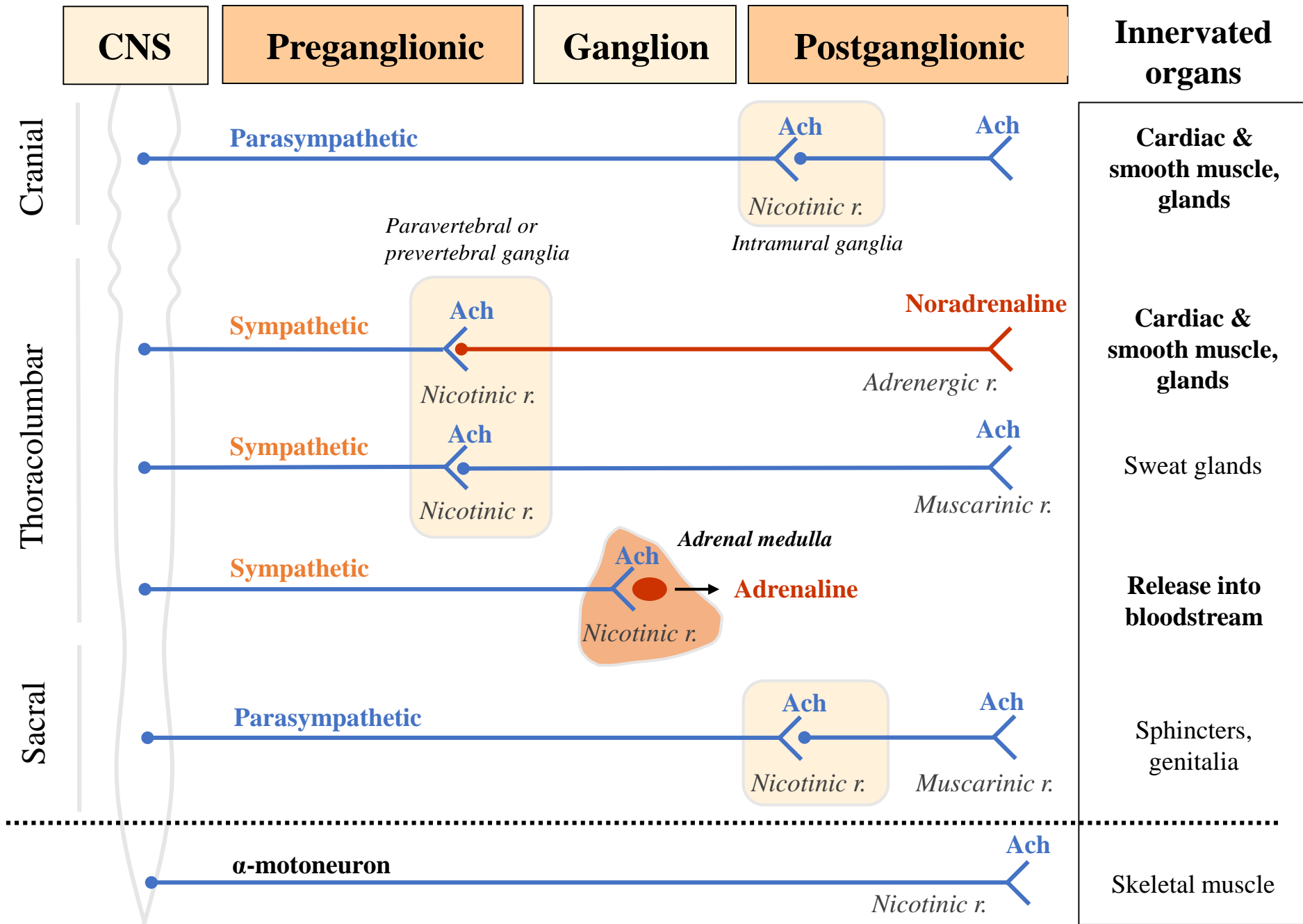
6. week

# Organization of nervous system



# Effects of VNS on organ systems

<i>Organ</i>	<i>Parasympathicus</i>	<i>Sympathicus</i>
HEART	↓ <b>rate</b>	↑ <b>rate</b> , ↑ <b>contractility</b>
VESSELS	----- ( <i>in some vessels vasodilation – NO mediated</i> )	<b>vasoconstriction – skin, splanchnic organs</b> vasodilation: <i>skeletal muscle, coronary arteries</i>
AIRWAYS	<b>bronchoconstriction</b>	<b>bronchodilation</b>
GIT	↑ <b>motility, secretion</b> sphincter relaxation	↓ <b>motility, secretion</b> sphincter contraction
PUPILS	<b>miosis</b>	<b>mydriasis</b>
SWEAT GLANDS	-----	↑ <b>secretion</b>
METABOLIC EFFECTS	-----	glycogenolysis, gluconeogenesis, lipolysis, renin secretion

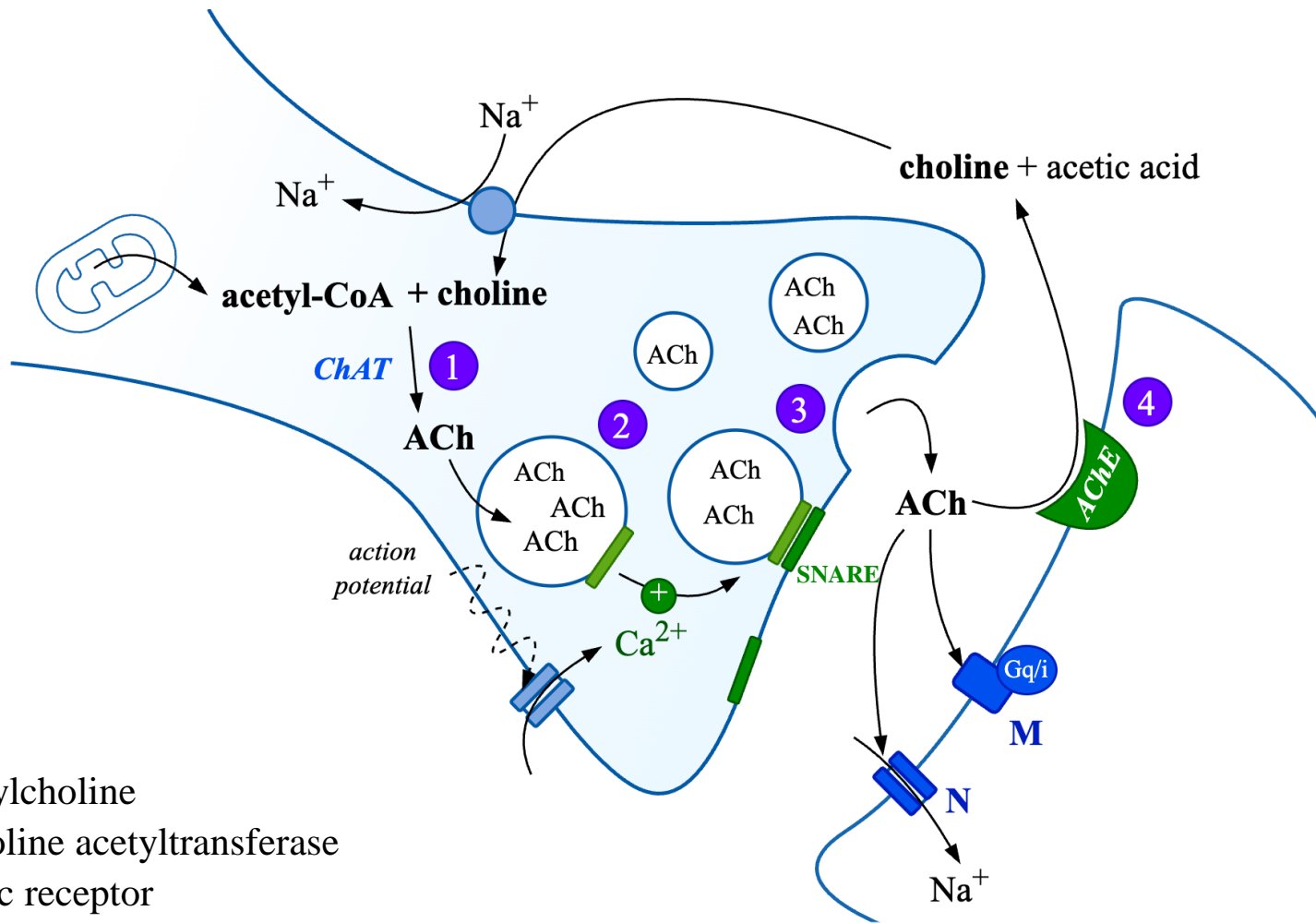


Ach = acetylcholine

# Metabolism of neurotransmitters

1. Synthesis
2. Storage in vesicles
3. Release into synaptic cleft
4. Degradation / reuptake

# Cholinergic synapse



**ACh** – acetylcholine

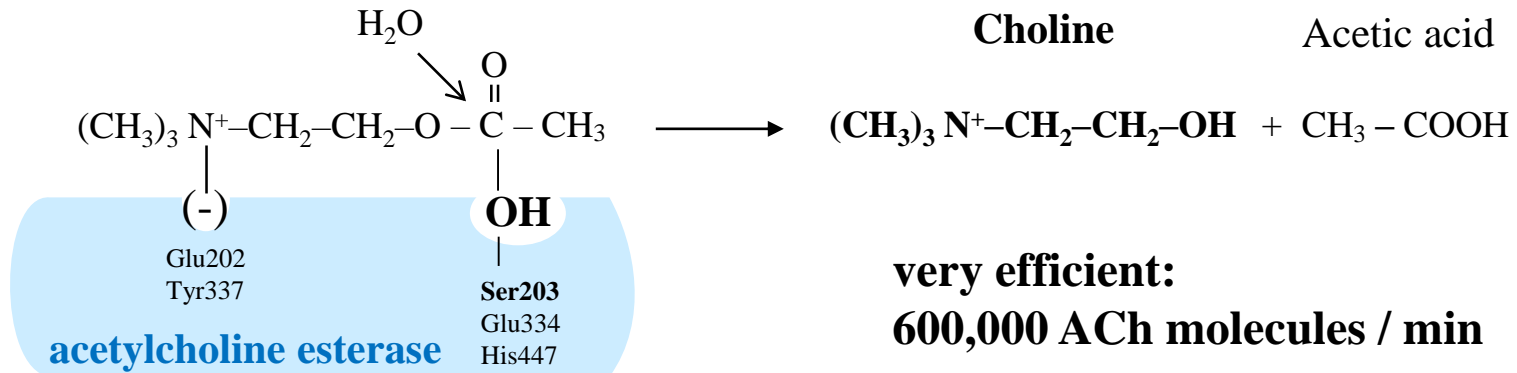
**ChAT** – choline acetyltransferase

**N** – nicotinic receptor

**M** – muscarinic receptor

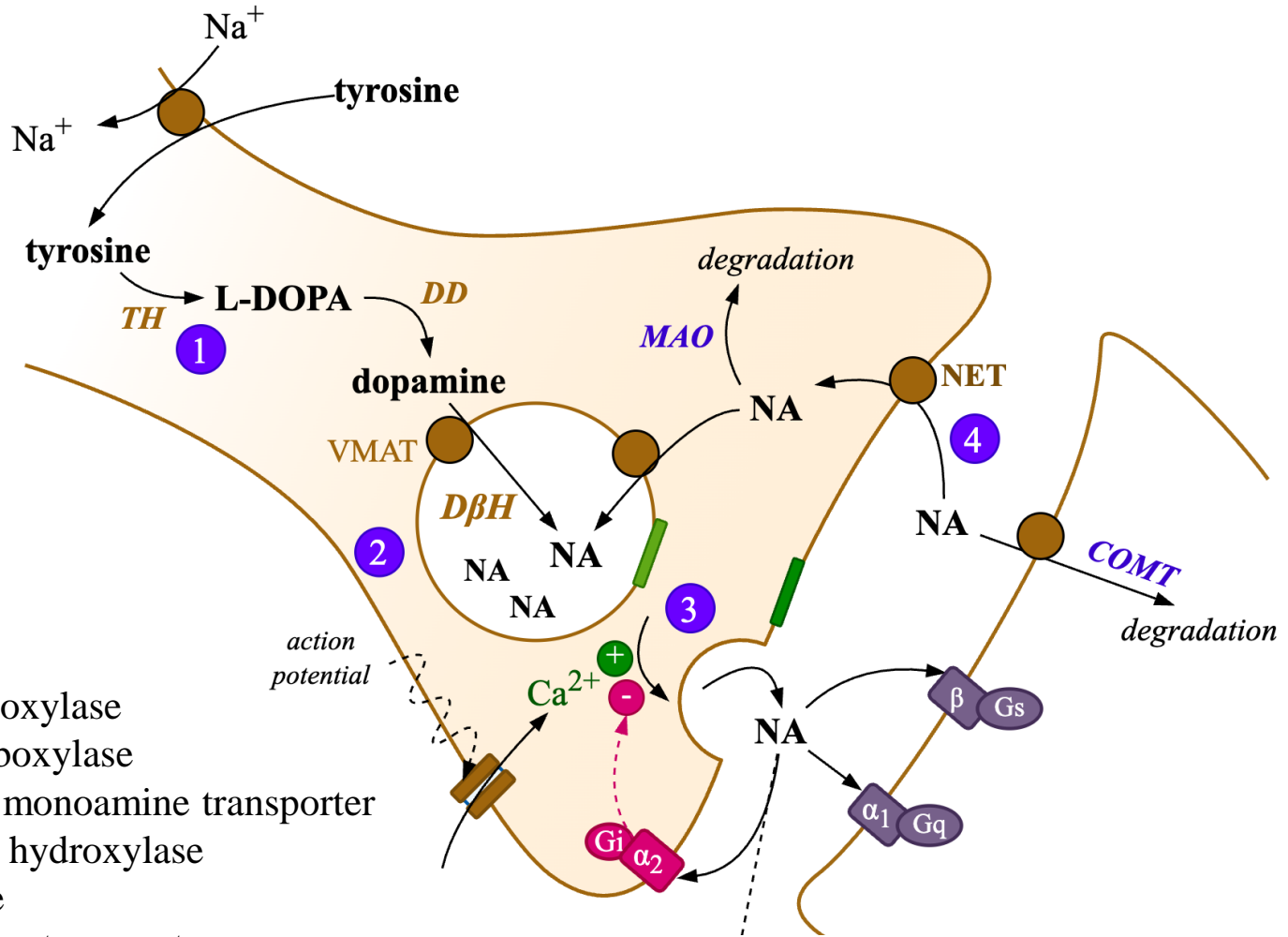
**AChE** – acetylcholinesterase

# Acetylcholine degradation



1. Binding of substrate (ACh)
2. Formation of a transient intermediate (involving – OH of serine 203)
3. Loss of choline and formation of acetylated enzyme
4. Deacetylation of AChE (regeneration of enzyme)

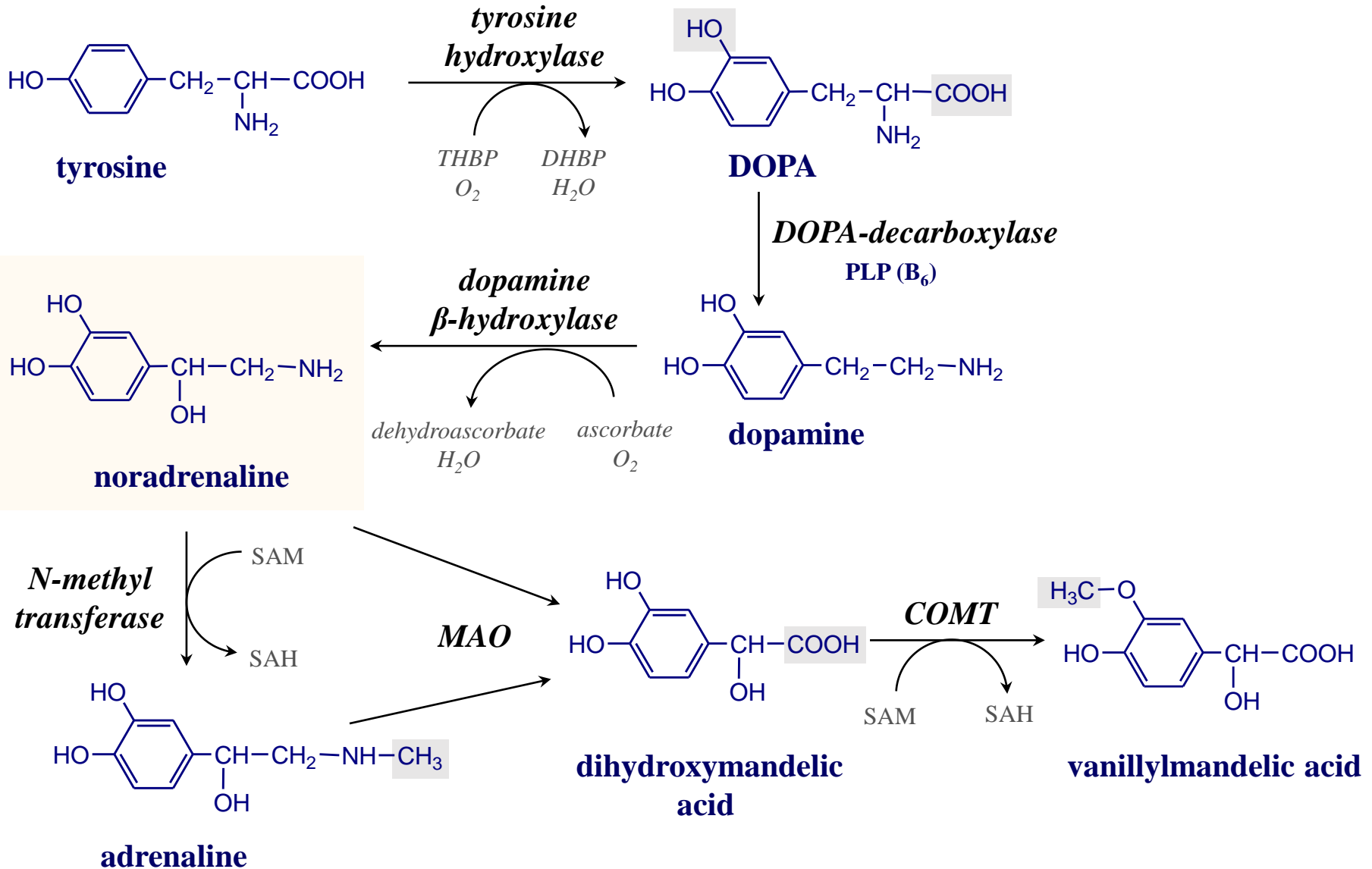
# Adrenergic synapse



- TH** – tyrosine hydroxylase
- DD** – DOPA-decarboxylase
- VMAT** – vesicular monoamine transporter
- DβH** – dopamine β hydroxylase
- NA** – noradrenaline
- NET** – noradrenaline transporter
- MAO** – monoamine oxidase
- COMT** – catechol-O-methyltransferase



# Synthesis and degradation of catecholamines



# Mechanisms of signal transduction

Effect of the signalling molecule depends on the presence of receptors

Receptors:

- **Intracellular** (for hydrophobic molecules)
- **Membrane** receptors:
  1. **Ionotropic**
  2. **Metabotropic:**
    - 2.1 G-protein coupled (GPCR)
    - 2.2 Enzyme-linked (catalytic)

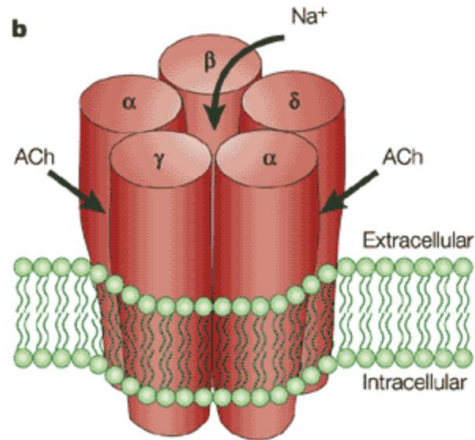
# Cholinergic receptors

## Nicotinic

- Ion channels
- Activated by **nicotine**



*Nicotiana  
tabacum*



## Muscarinic

- G-protein coupled
- Activated by **muscarine**

*Fly agaric -  
Amanita muscaria*



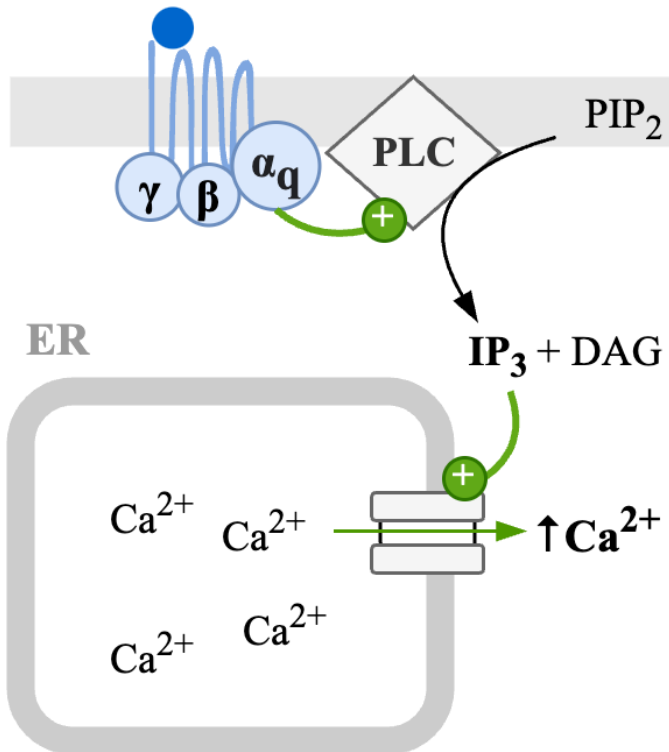
- Inhibited by **atropine**



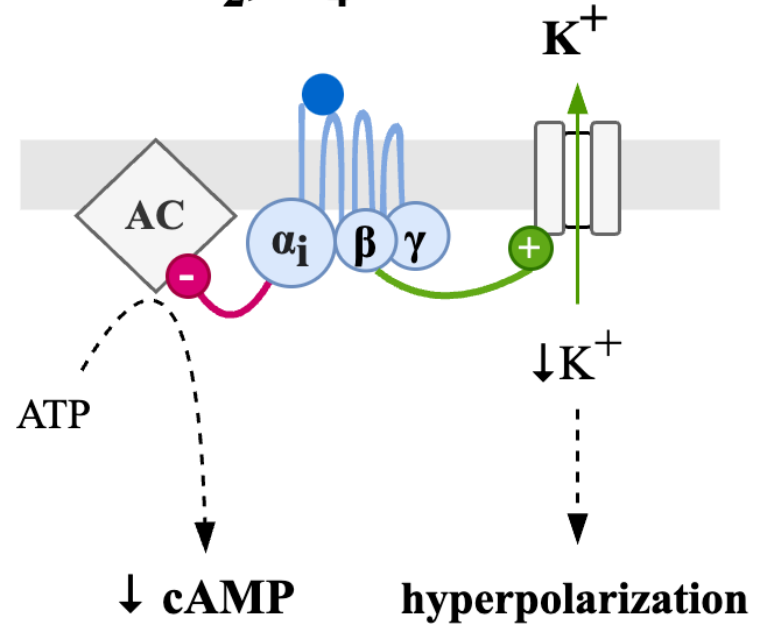
*Deadly nightshade  
- Atropa  
belladonna*

# Cholinergic receptors - muscarinic

**M<sub>1</sub>, M<sub>3</sub>, M<sub>5</sub>**



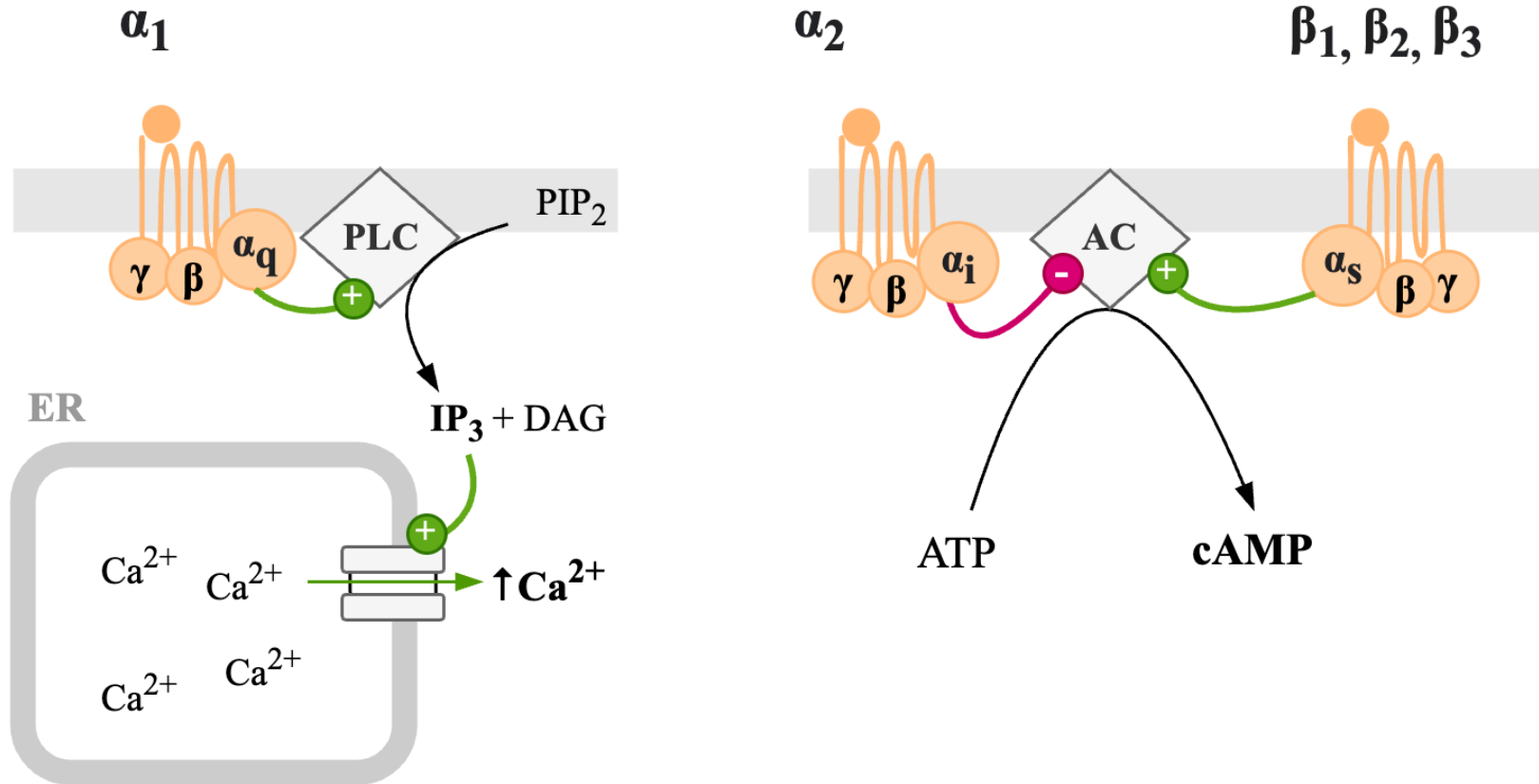
**M<sub>2</sub>, M<sub>4</sub>**



# Cholinergic receptors

receptor	ligand	signalling	location	function
$N_N$	ACh	ion channel (Na <sup>+</sup> )	postganglionic neurons – both sympathetic and parasympathetic	<b>postganglionic neuron activation</b>
$N_M$	ACh	ion channel (Na <sup>+</sup> )	neuromuscular junction	contraction of skeletal muscle
$M_1, M_3, M_5$	ACh	$G_{q(p)}$	<b>GIT (glands) airway smooth muscle (CNS)</b>	<b>↑ secretion bronchoconstriction</b>
$M_2 (M_4)$	ACh	$G_i$	<b>SA node, atria, (CNS)</b>	<b>↓ heart rate</b>

# Adrenergic receptors



# Adrenergic receptors

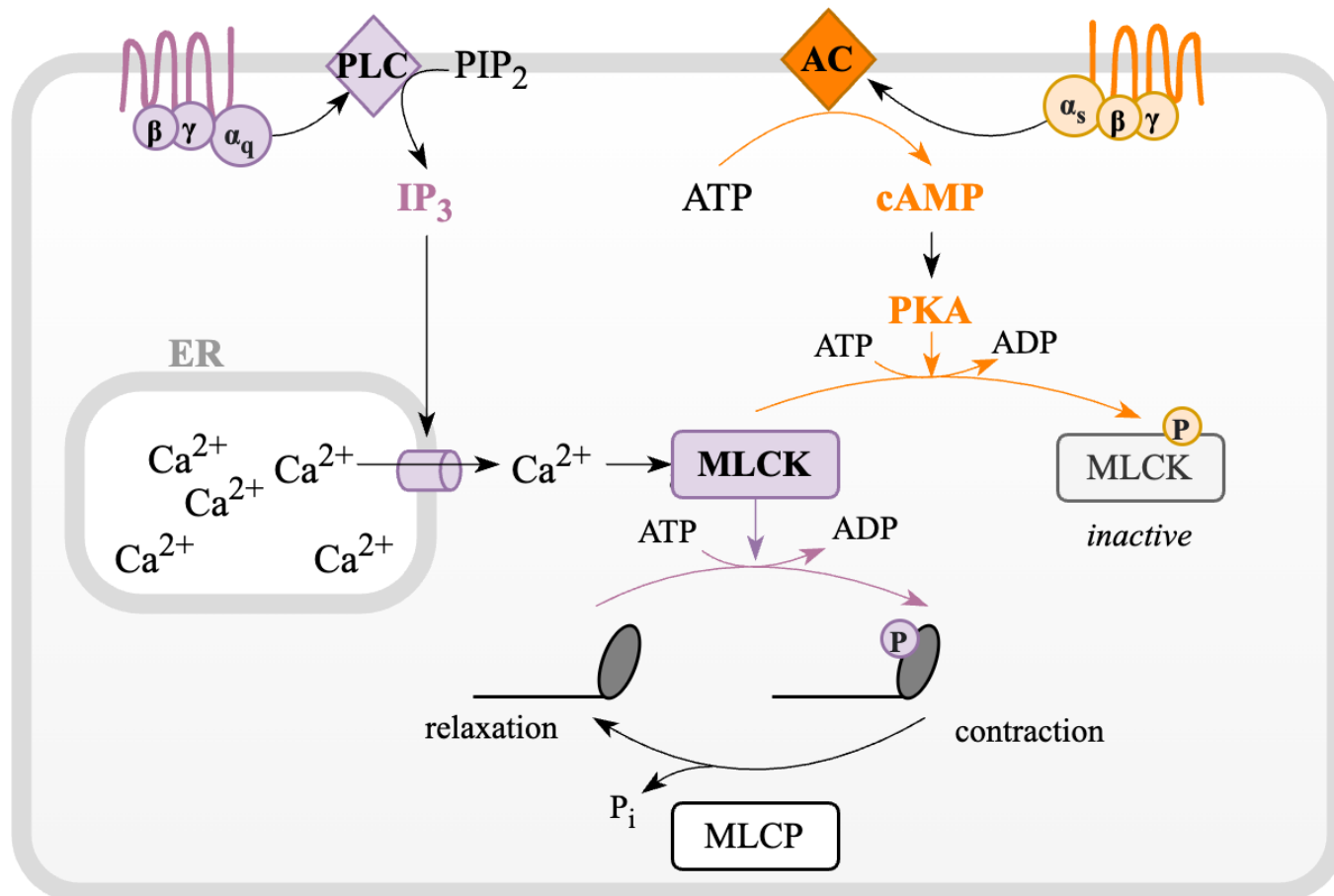
receptor	ligand	signalling	location	function
$\alpha_1$	NA>A	G <sub>q (p)</sub>	vascular smooth muscle (skin, GIT)	<b>vasoconstriction</b>
$\alpha_2$	NA>A	G <sub>i</sub>	<b>presynaptic neurons</b>  platelets	<b>feedback regulation of neurotransmitter release</b>  platelet aggregation
$\beta_1$	A=NA	G <sub>s</sub>	<b>myocardium</b>  juxtaglom. apparatus	<b>↑ rate, ↑ contractility, ↑ relaxation of cardiac muscle</b> ; renin secretion
$\beta_2$	A>NA	G <sub>s</sub>	<b>airway smooth muscle</b>  skeletal muscle and coronary arteries <b>liver</b>	<b>bronchodilation</b>  vasodilation  <b>↑ glucose production</b>
$\beta_3$		G <sub>s</sub>	<b>adipose tissue</b>	<b>↑ lipolysis</b>

# Effect of VNS on airway and vascular smooth muscle

$\alpha_1$  - vascular smooth muscle (skin, GIT)

$M_3$  - airway smooth muscle

$\beta_2$  - airway smooth muscle,  
coronary arteries, skeletal muscle

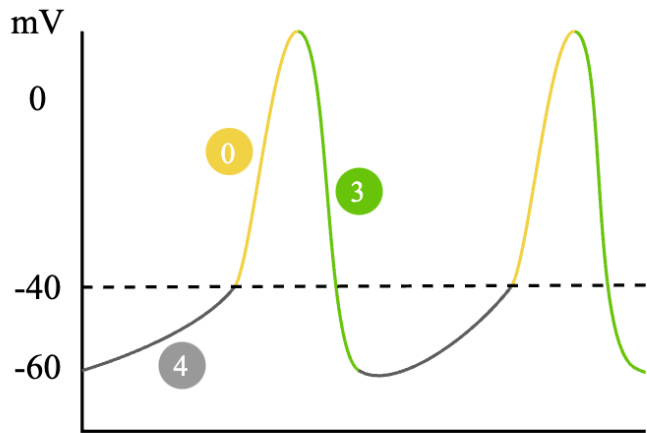


**MLCK** – myosin light chain kinase

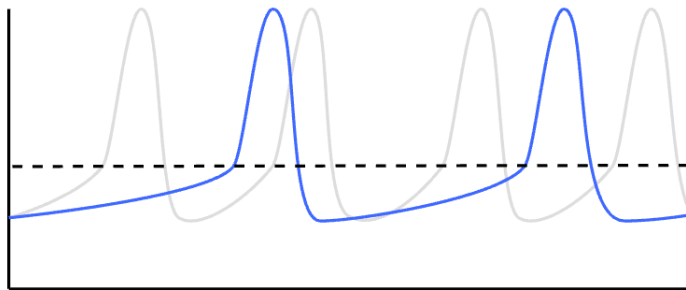
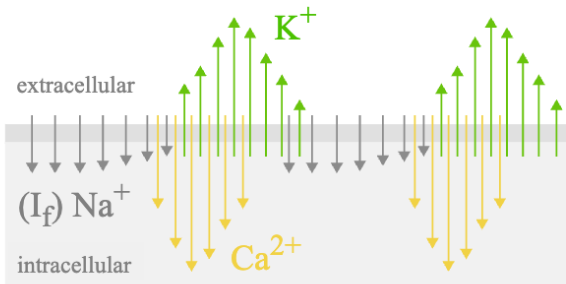
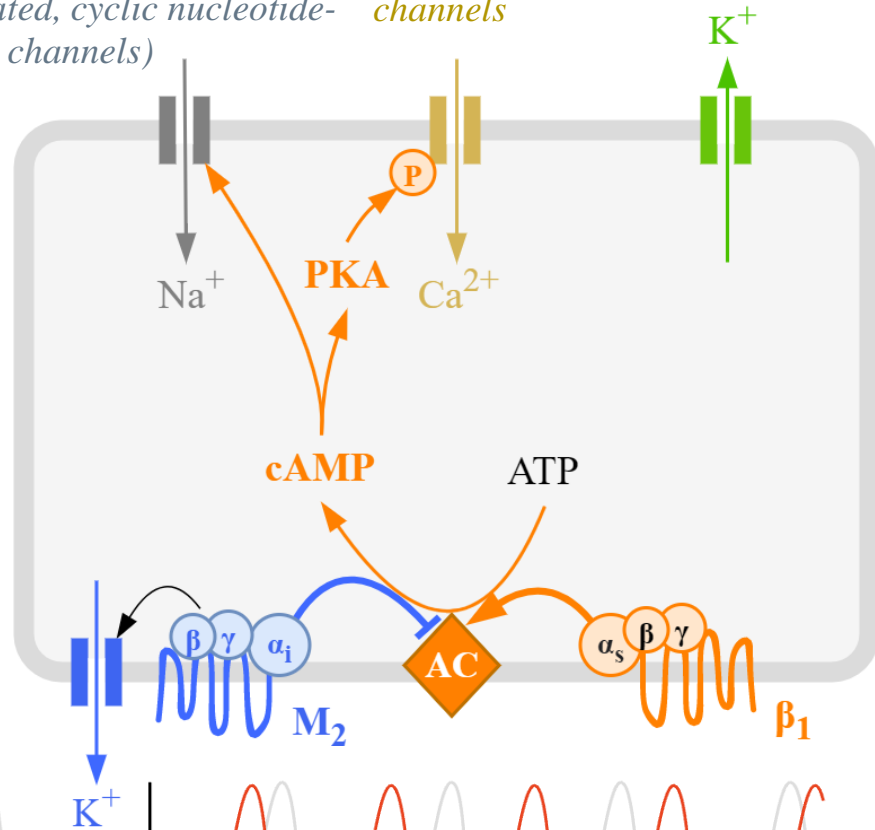
**MLCP** – myosin light chain phosphatase



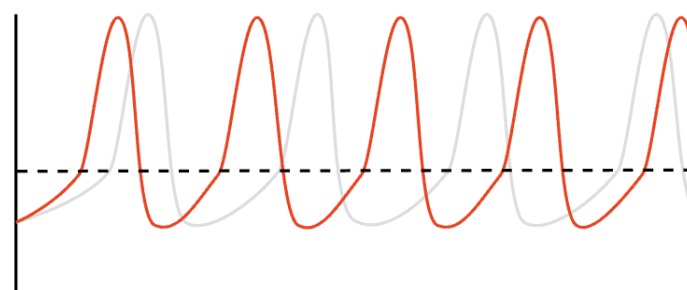
# Effect of VNS on SA node



*HCN (hyperpolarization activated, cyclic nucleotide-gated channels)*      *L-type  $Ca^{2+}$  channels*

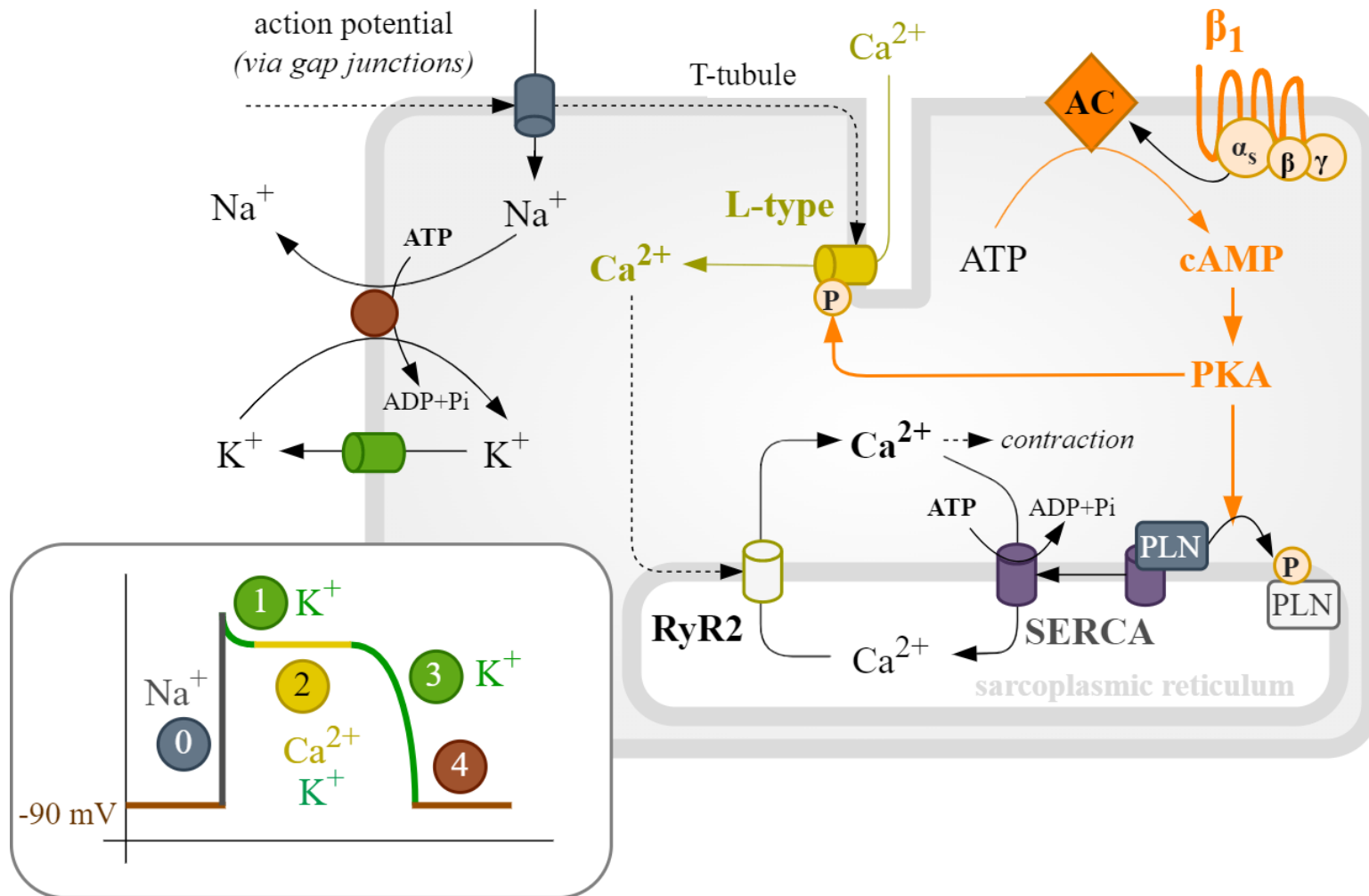


**parasympathetic – ↓ heart rate**



**sympathetic – ↑ heart rate**

# Effect of VNS on myocardial contraction



**PKA** – proteinkinase A, **PLN** – phospholamban, **RyR** – ryanodine receptor, **SERCA** – sarco/endoplasmic reticulum Ca<sup>2+</sup> ATPase