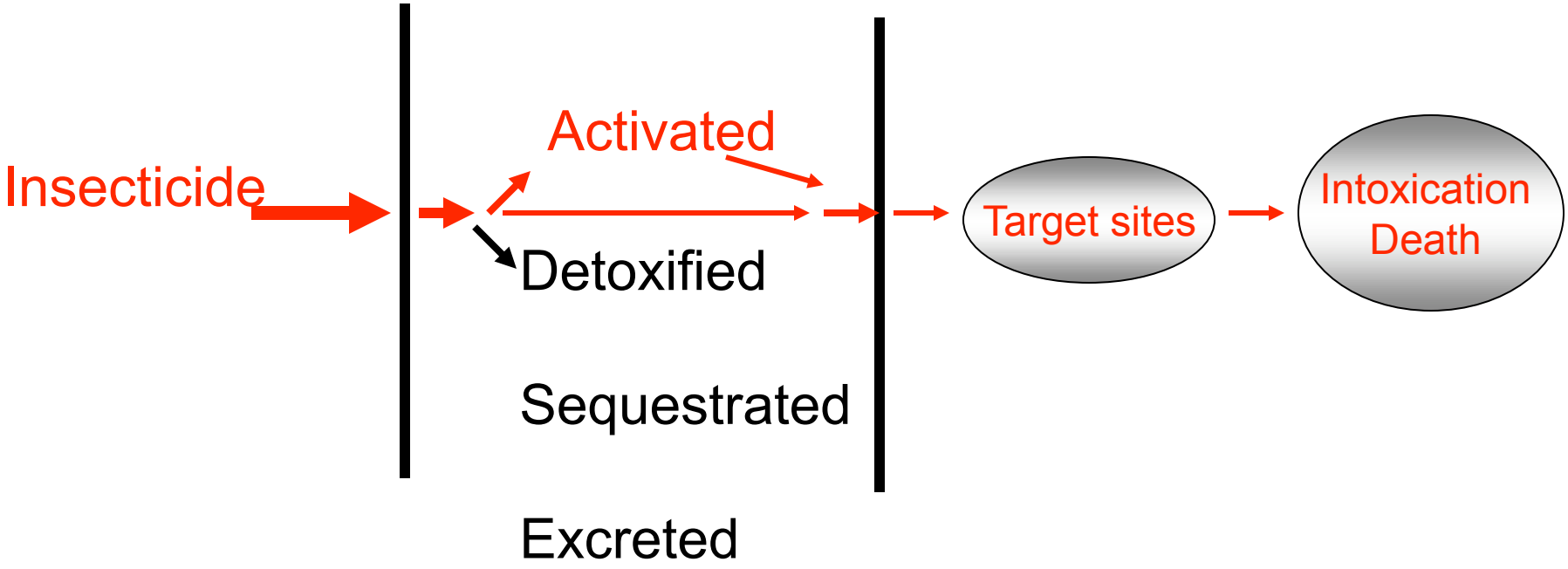
Insect Toxicology

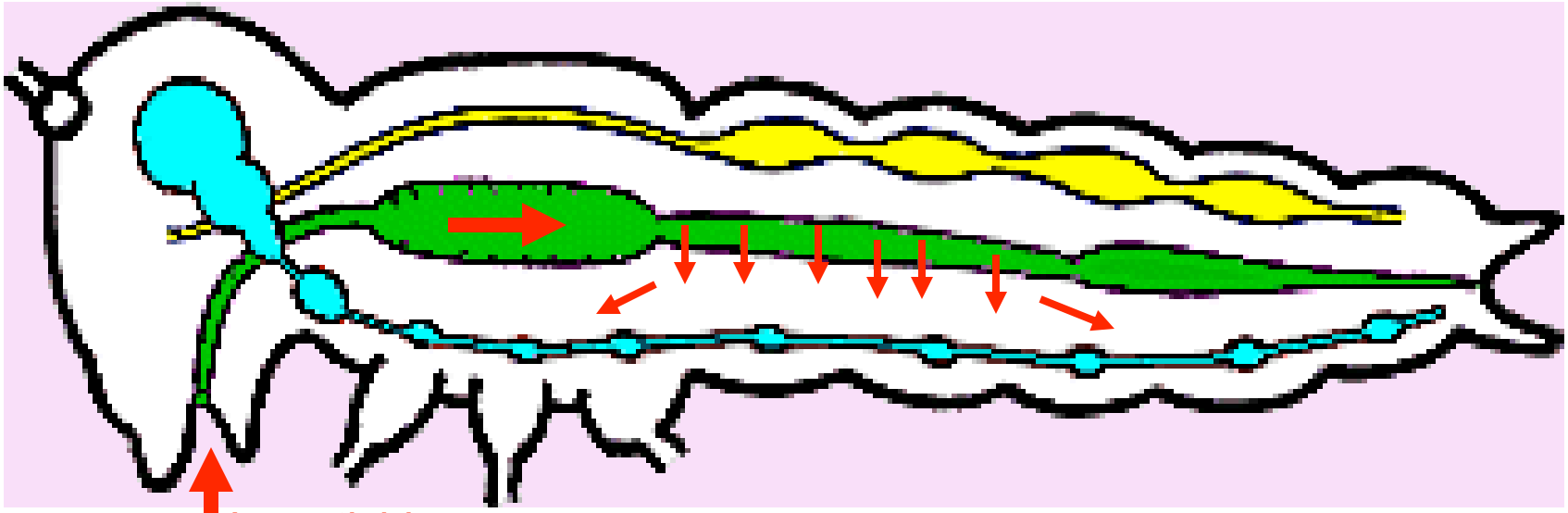
The general toxicological process



outlines

- Mode (route) of entry
- Metabolism & excretion
- Mode of action: interaction with target sites

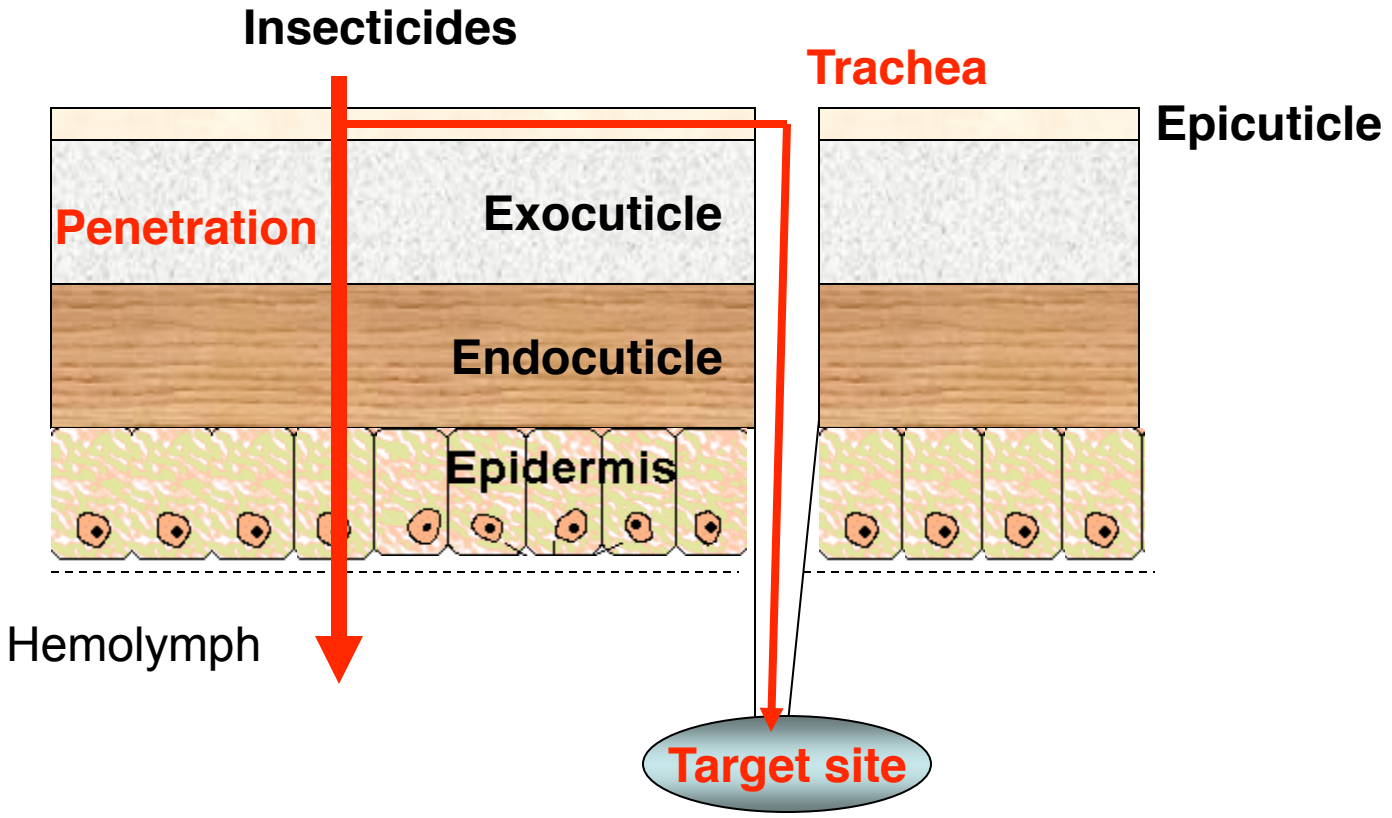
Mode of entry: stomach



Insecticides

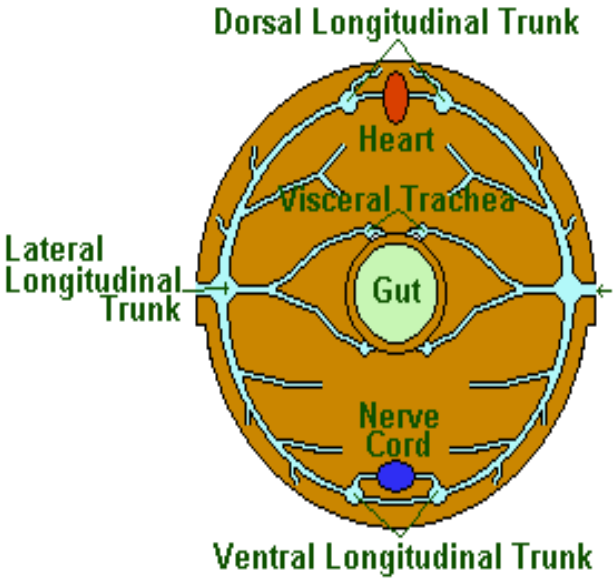
Stomach poison (insecticide): Bt toxin

Mode of entry: integument

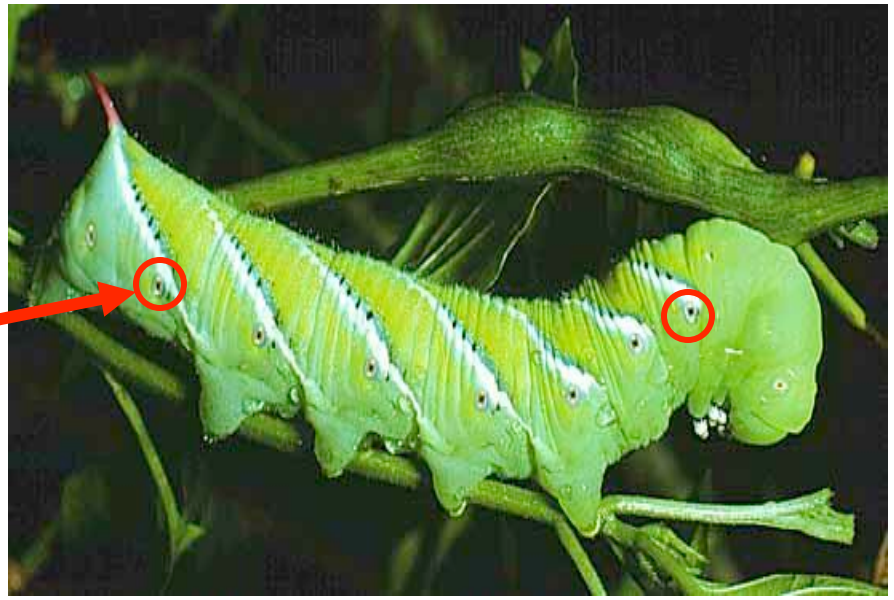


Contact poison (insecticide)

Mode of entry: spiracle and trachae



Spiracle



Fumigant: volatile at normal temperature

Mode of entry: systemic transport

- Some insecticides (usually polar) can penetrate plant tissues and be translocated to the other parts of plants via xylem and/or phloem
- Sucking mouthpart pests such as aphids and whiteflies “drink” pesticides while they suck up plant juice
- Otherwise similar to stomach entry.
- Systemic poison (or insecticide)

Mode of entry: summary

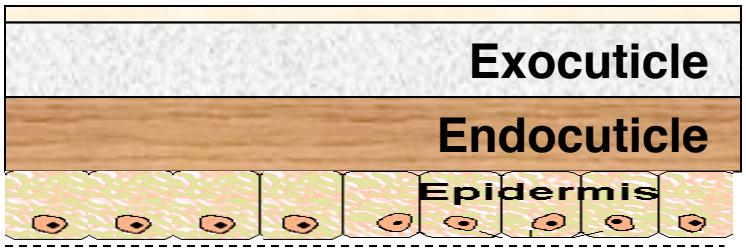
- Stomach poison: enter through mouth and midgut. (Bt)
- Contact poison: Most insecticides enter through the cuticle
- Fumigant: volatile insecticides enter through the spiracle and tracheal system. (phosphine, methyl bromide etc.)
- Systemic poison: relatively polar insecticides are absorbed and translocated by plants. Enter insects through mouth and midgut along with plant juice

Metabolism & excretion

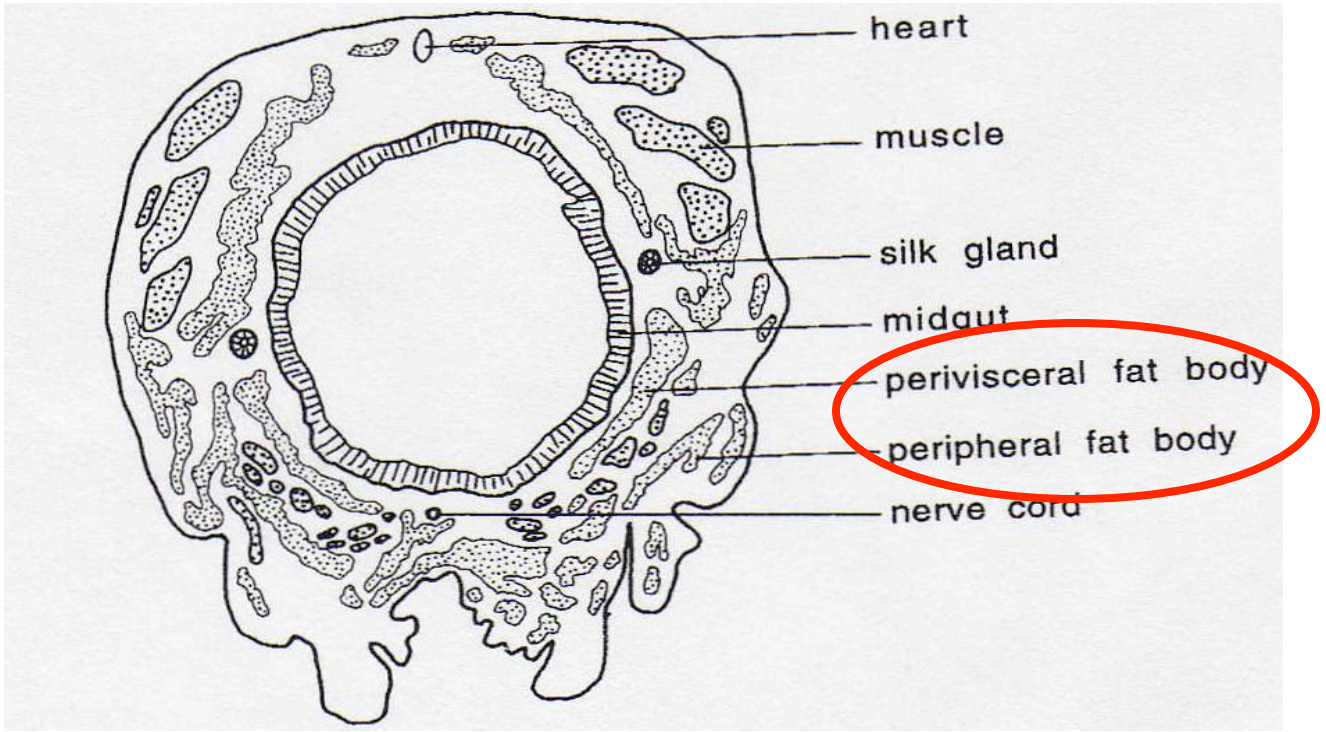
- Bioavailability: the percentage of insecticides that is available to the corresponding target sites inside the insect body .
- Not all insecticides entered inside pest body are available to their target sites. because of:
  - Sequestration
  - Direct excretion
  - Metabolism

Sequestration

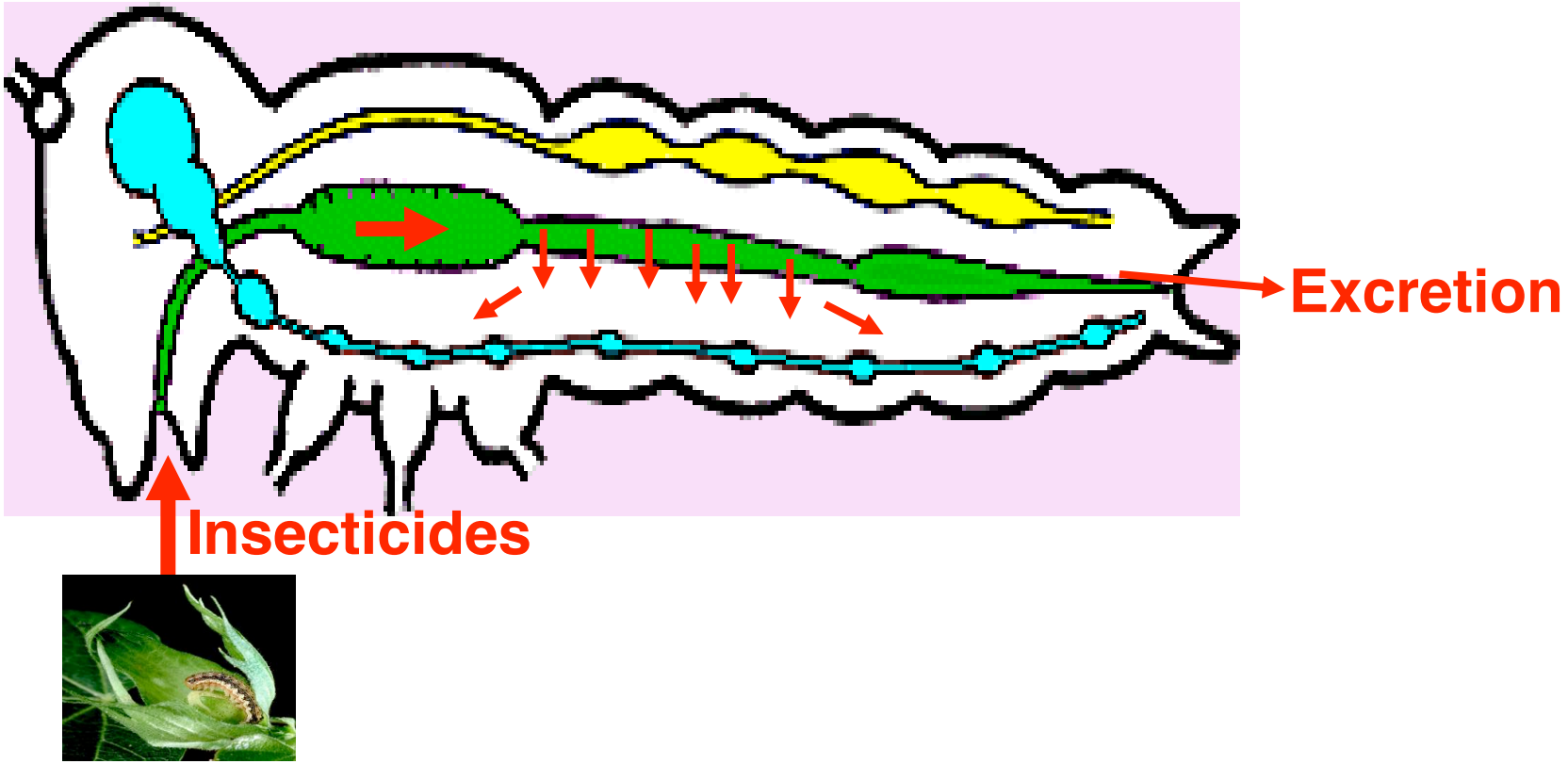
- **Integument**



- **Fatbody**



Direct excretion



Metabolism and detoxification

- Oxidation: Cytochrome P450 monooxygenases. Usually results in detoxifications, but sometimes (esp. S-oxidation) activate the pesticides. Detoxify all classes of insecticides

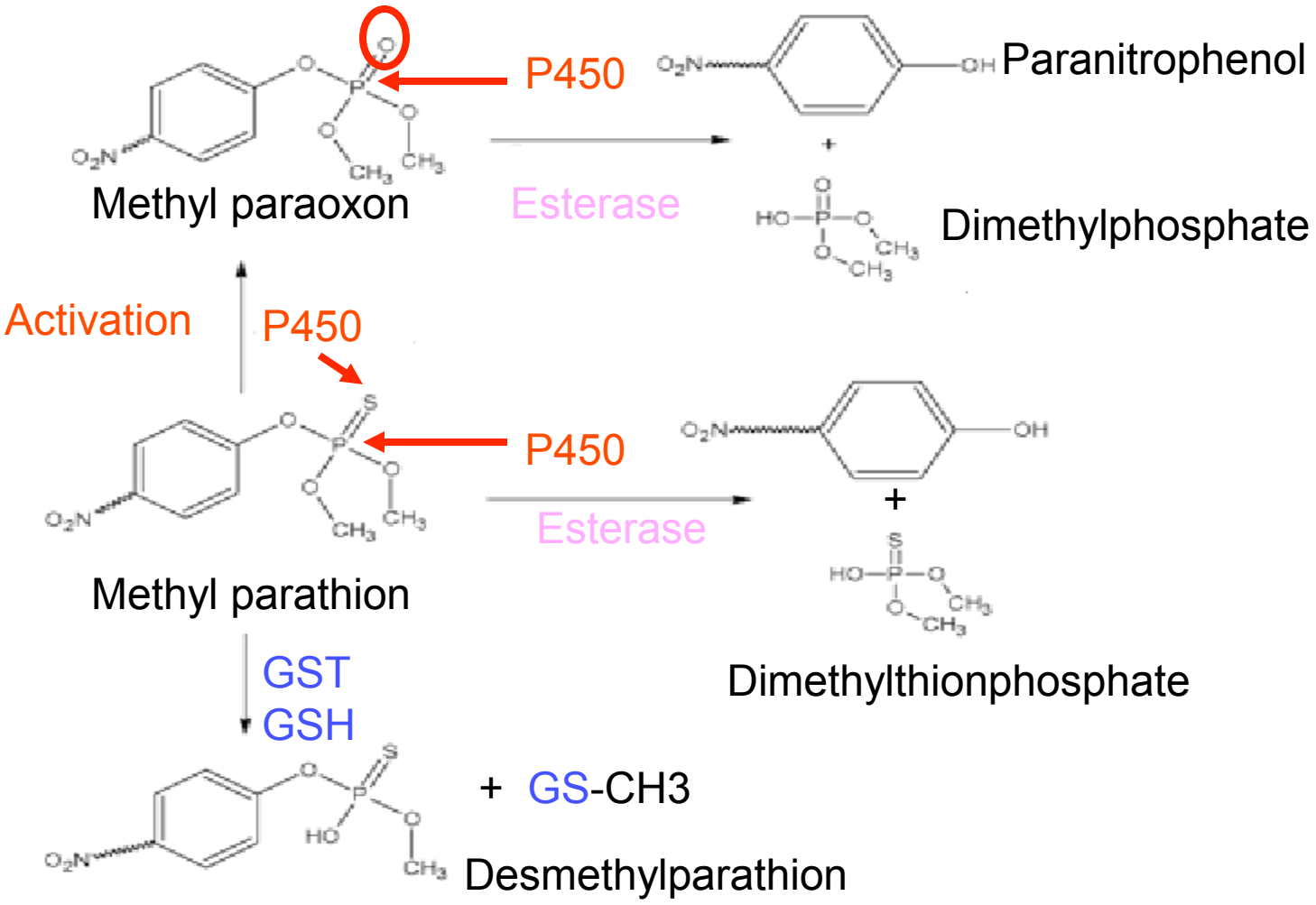
- Hydrolysis: Esterases. Result in detoxifications. Detoxify organophosphates (OP), carbamates (Carb), and Pyrethroids (Py)

- Reduction: not common.

- Conjugation: pesticide or its metabolites are conjugated to either glucose or glutathione (GSH) and become more water soluble and more easily excreted.

  Glutathione-S-transferase (GST): catalyzing conjugation with GSH. Detoxify DDT, OP and Py

P450, GST and Esterase work together



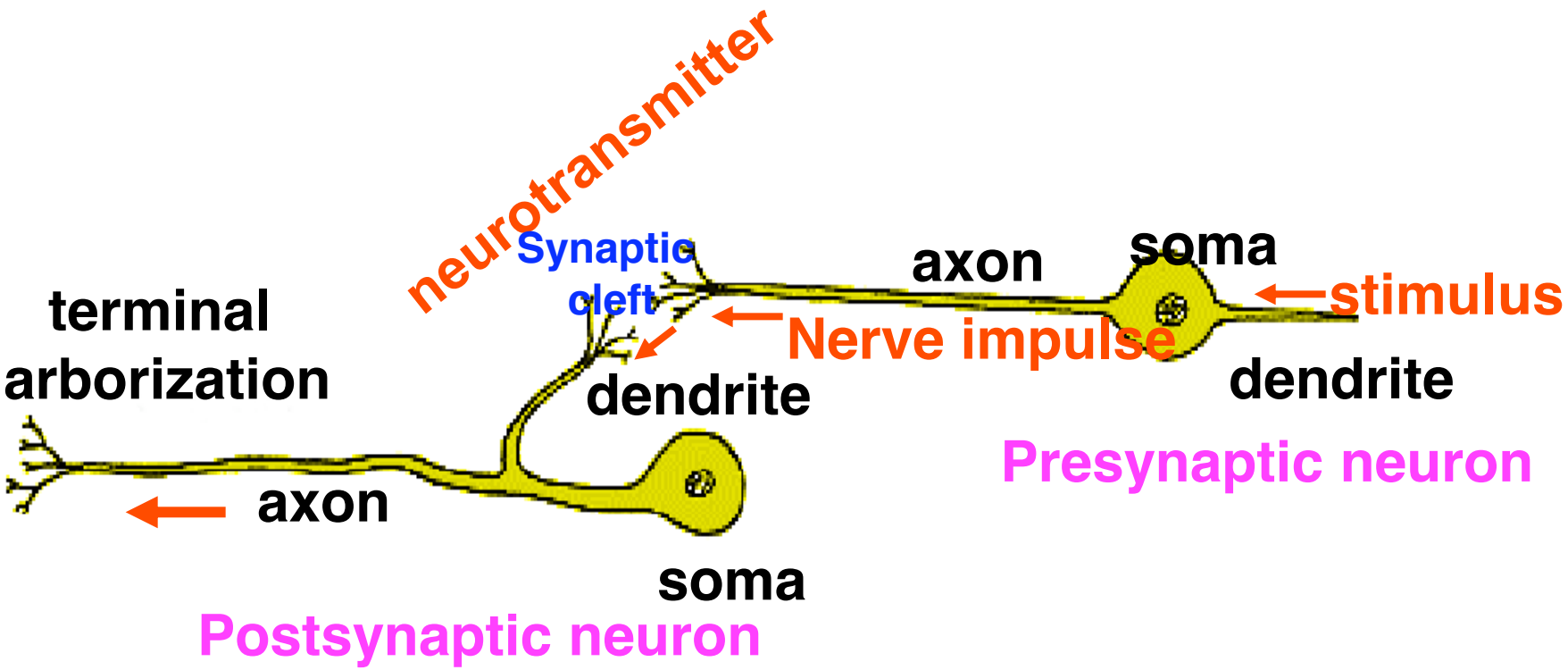
Mode of action: interaction with target sites

- Neurotoxins: Nerve system
  - Rapid knock down and kill insects
  - Relatively broad spectrum
  - Lower selectivity
- IGR: Insect growth regulator
  - Endocrine system
  - Chitin synthesis (integument)
  - Slow, disrupt normal growth (and reproduction)
  - Soft, selective

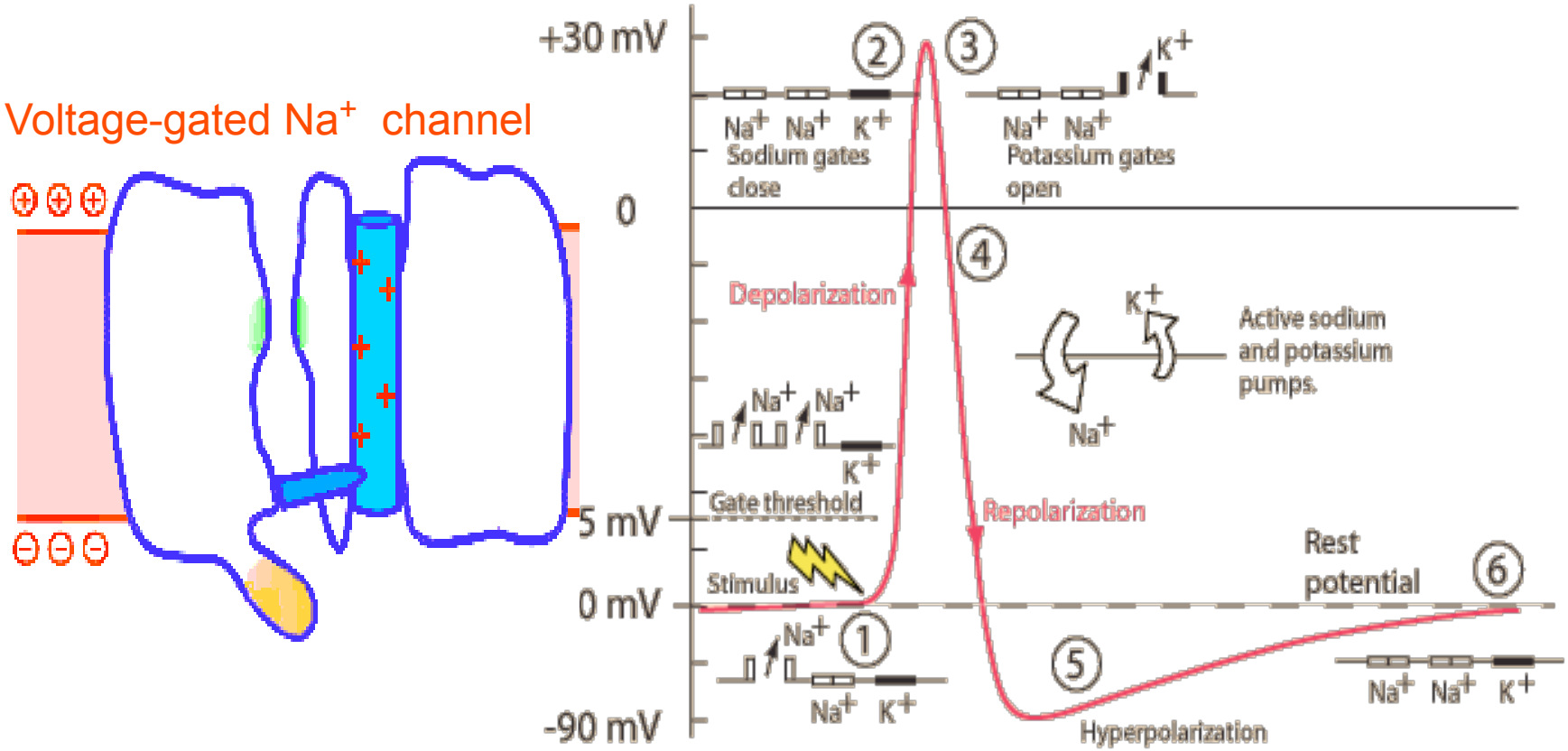
Mode of action: nerve system

- Signal (sensory) transduction
- Axon transmission
- Synaptic transmission

Neurotoxins: Quickly knock down and Kill insects

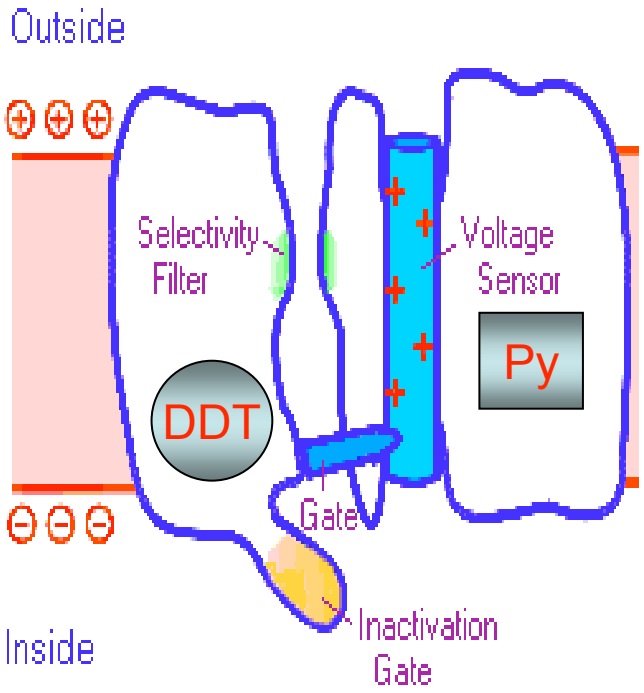


Mode of action: axon transmission

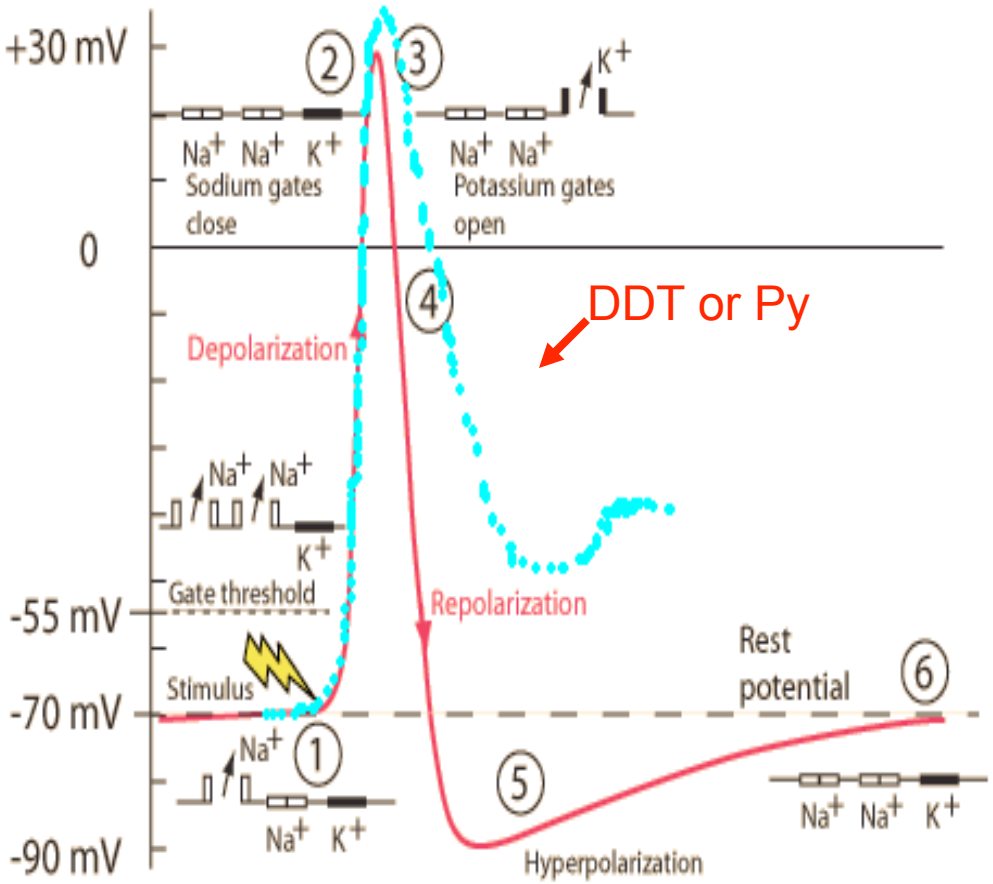


Action Potential (AP)

Voltage-gated Na+ channel modulators: DDT and pyrethroids (Py)

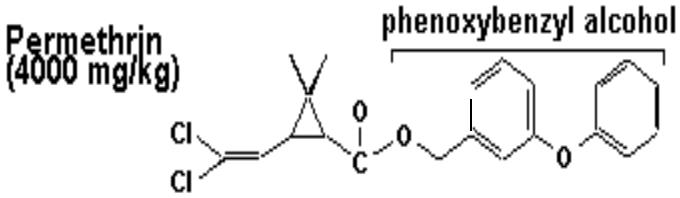


DDT or Py bind to Na+ channel

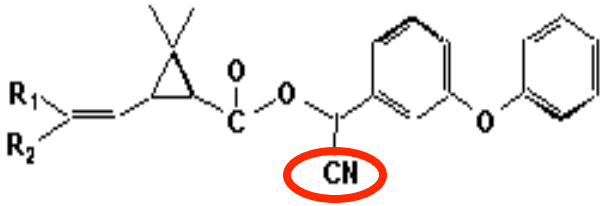


Voltage-gated Na+ channel modulators: DDT and pyrethroids

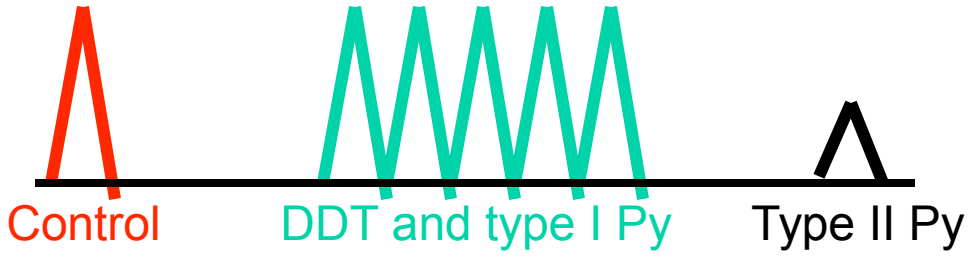
• DDT and type I Py: slowing Na+ channel closing, negative after potential >Na+ gate threshold, resulting multiple repetitive action potential (firing), hyperexcitation, tremor, lose of coordination (knock down), paralysis, death.



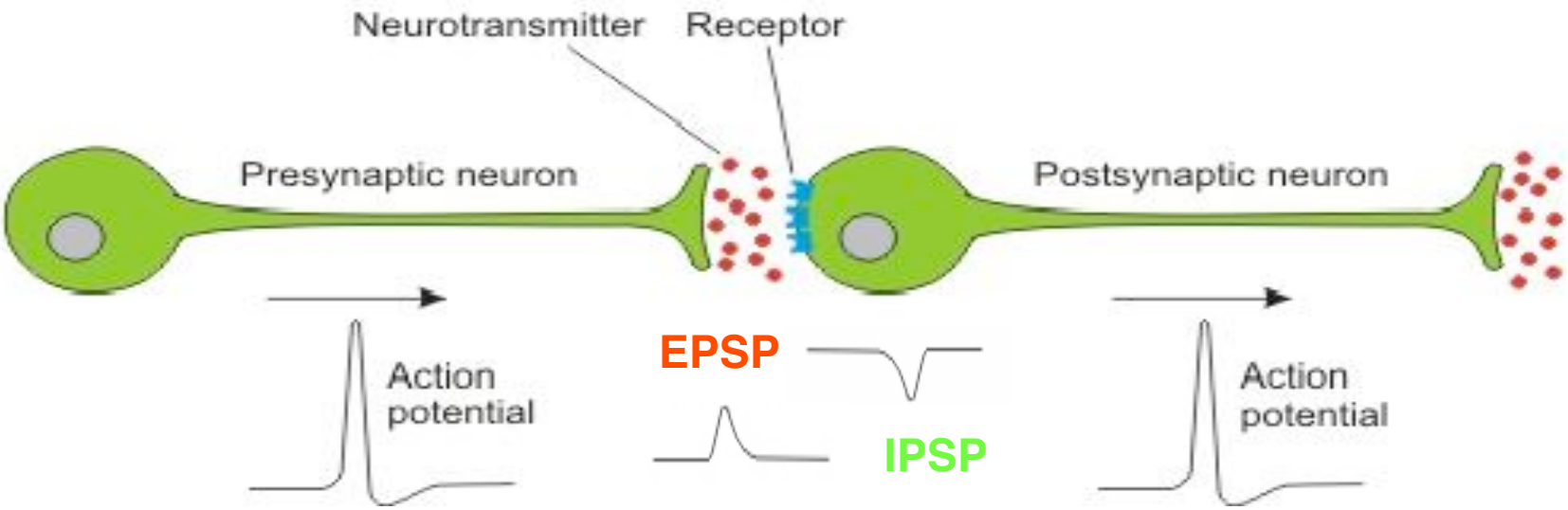
• Type II Py: preventing Na+ channel from closing, action potential repressed, Rapid knock down, paralysis, and then death.



Cypermethrin: $R_1 = R_2 = Cl$ (250 mg/kg)

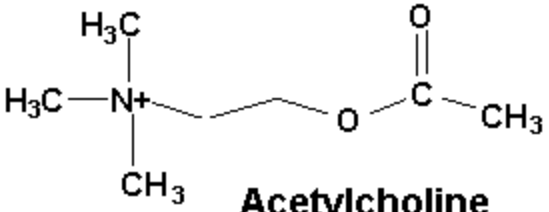


Mode of action: synaptic transmission

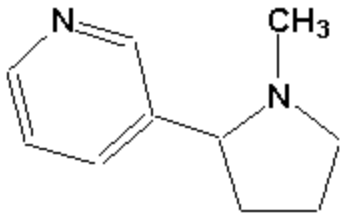


- Acetylcholine (Ach), Ach receptor (AchR), Acetylcholine esterase (AchE)
- ɣ-amino butyric acid (ɣ GABA), ɣ GABA-gated Cl^- channel (= ɣ GABA receptor)
- Octopamine (OA), OA receptor (GPCR)

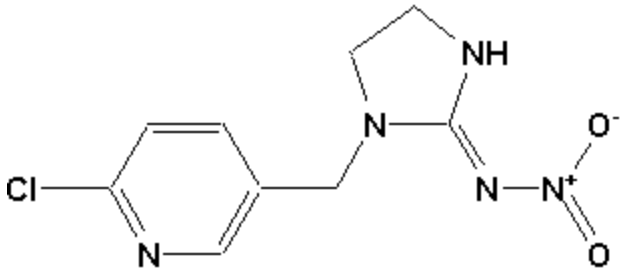
AchR agonists: Neonicontinoids and Spinosad



Acetylcholine

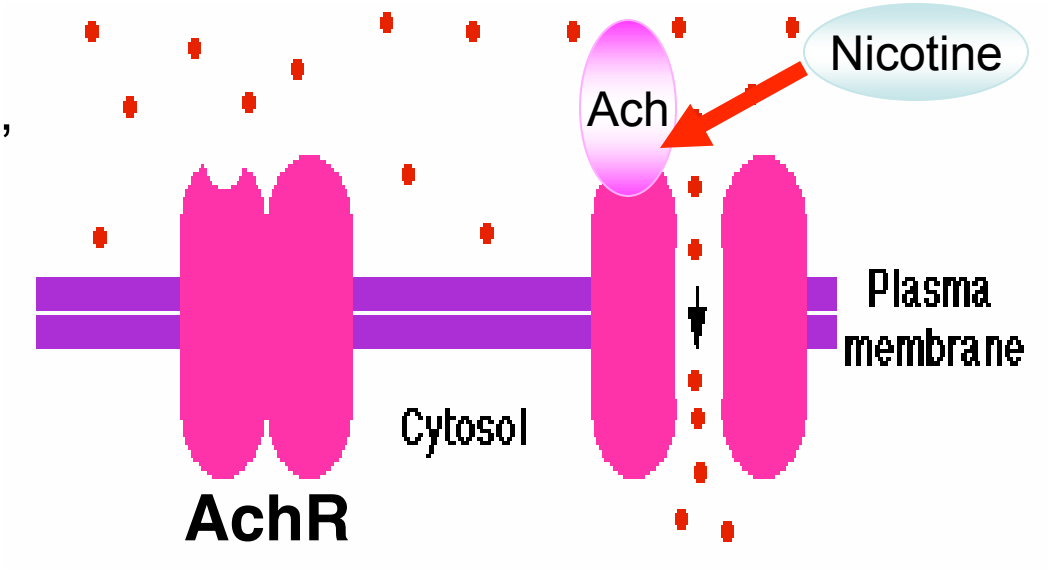


Nicotine (55 mg/kg)

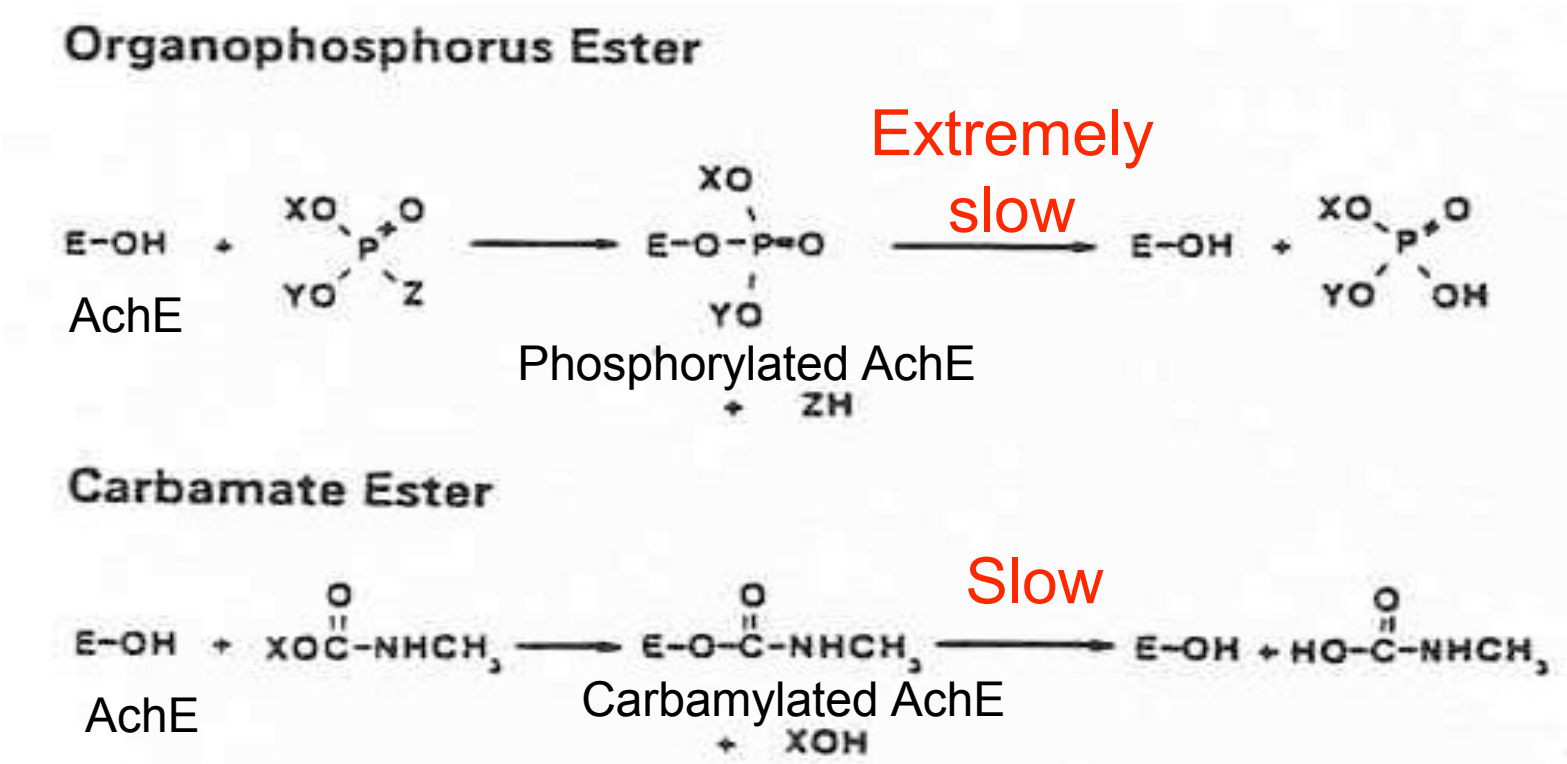


Imidacloprid (424-475 mg/kg)

- Neonicontinoids and spinosad can bind to AchR, leading to Overstimulation, tremor, paralysis and death
- Selective (aphids, whitefly and some moth)
- low affinity to vertebrate AchR

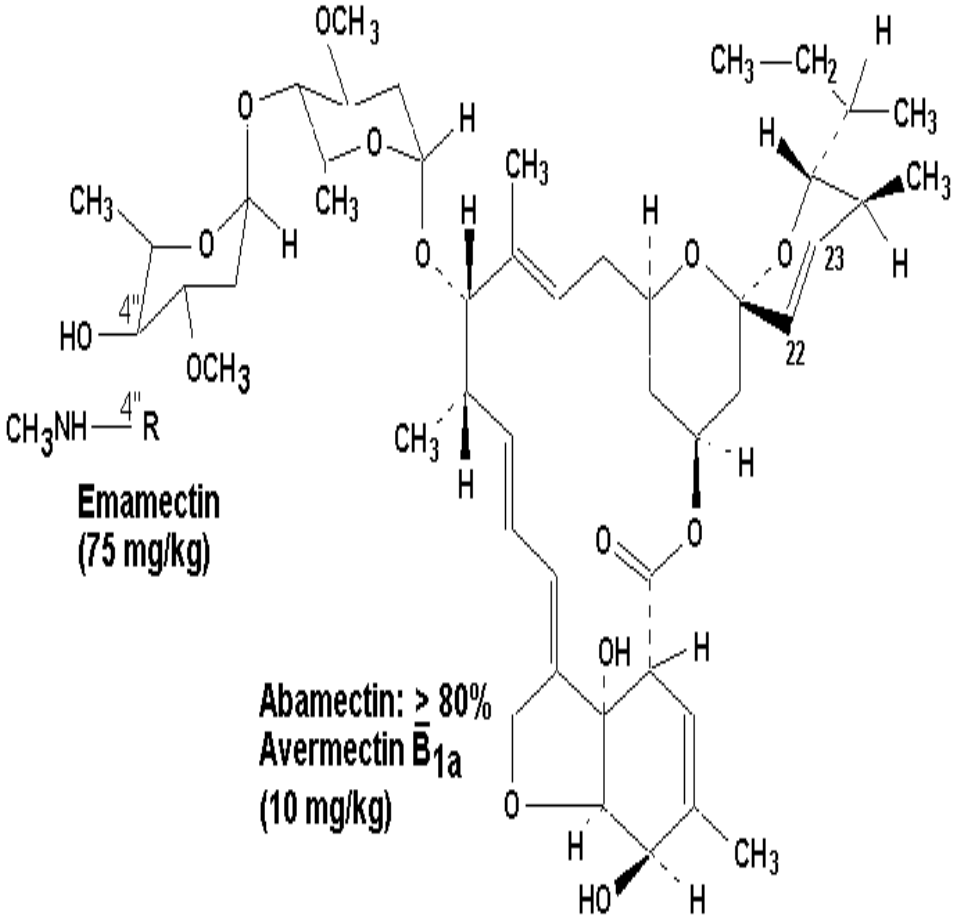


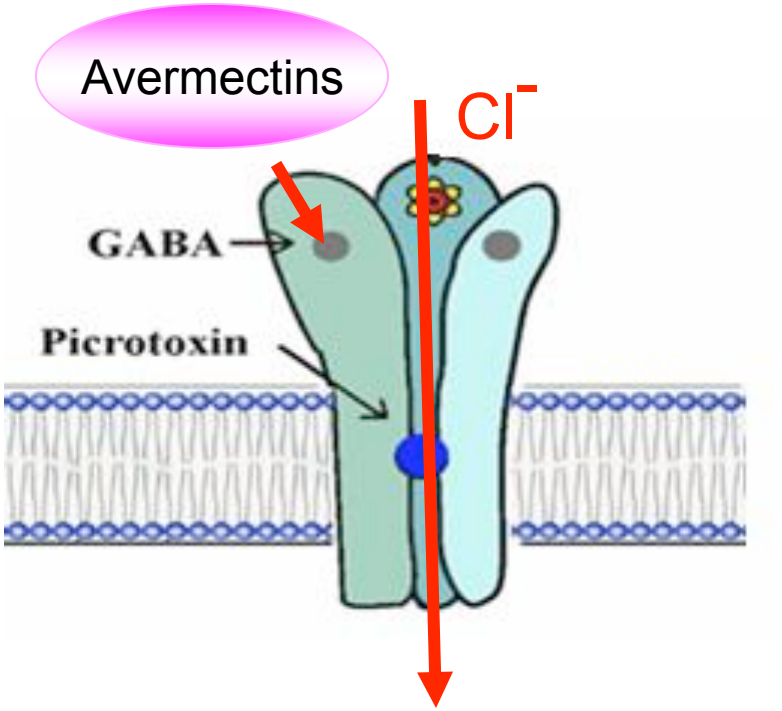
AchE inhibitors: OP and Carb



- Hyperexcitation, death by respiratory failure
- Broad spectrum in activity
- Low selectivity between human and insects

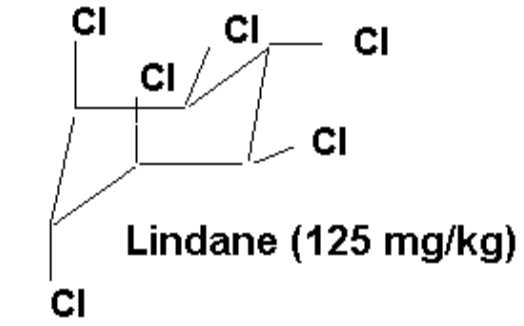
GABA receptor agonists: avermectins



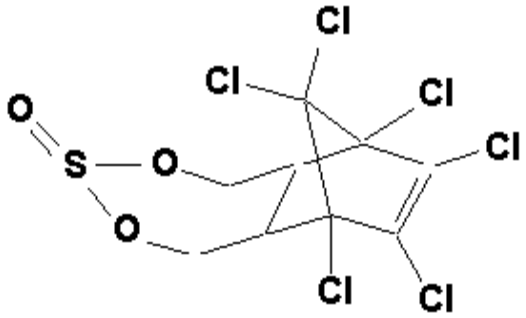


Ataxia, paralysis, death

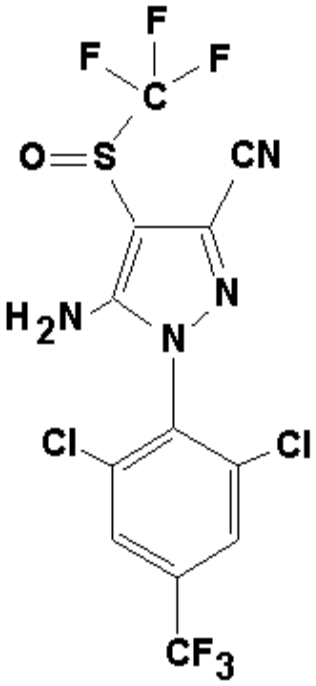
GABA receptor antagonist: cyclodiens and fipronil



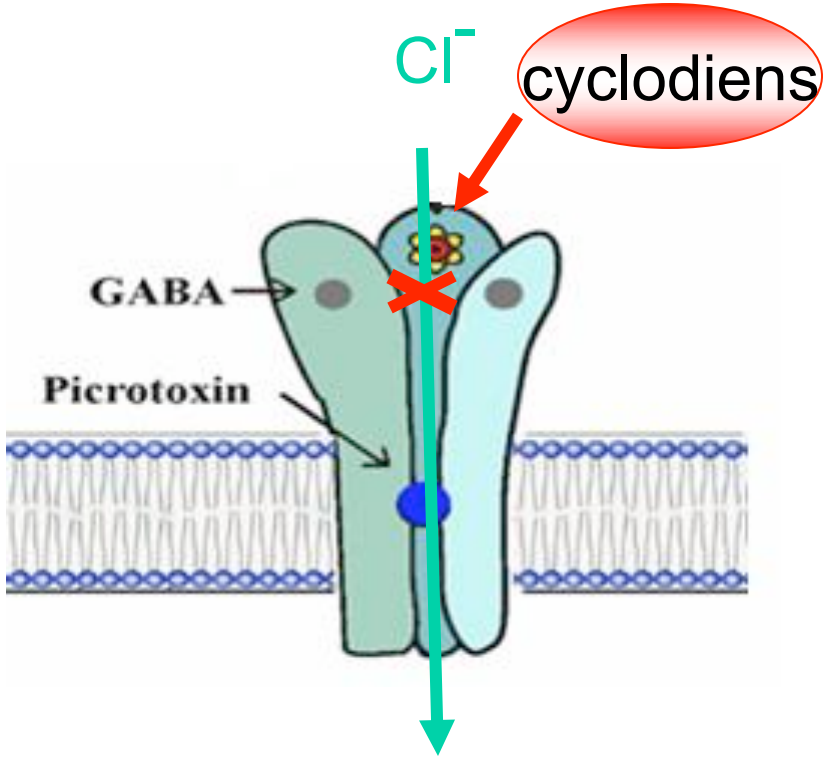
Lindane (125 mg/kg)



Endosulfan
(23-160 mg/kg)

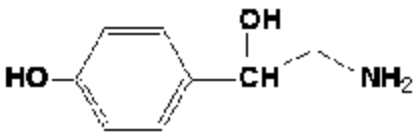


Fipronil
(95 mg/kg oral;
>2000 mg/kg dermal)

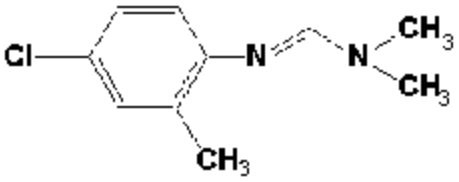


Block the effects of GABA, leading to hyperexcitation

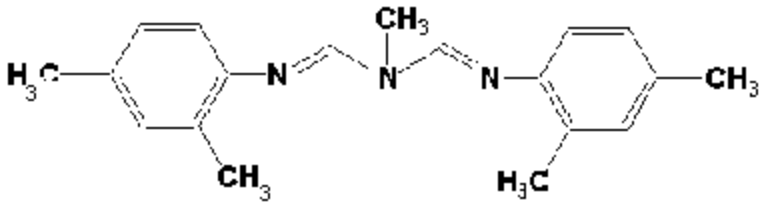
OA receptor agonists: Formamidines



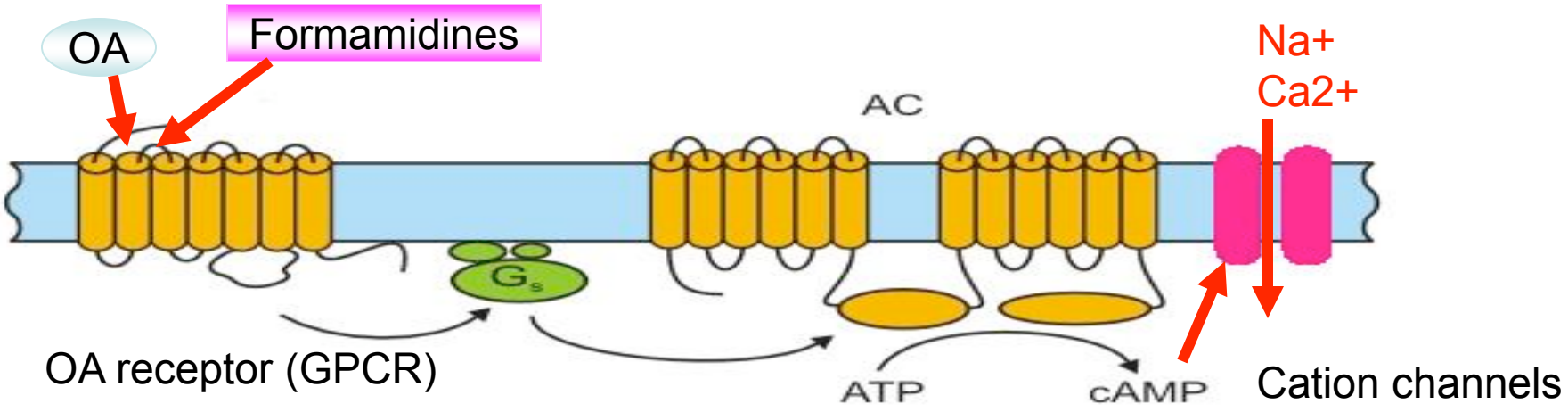
Octopamine (OA)



Amitraze



Chlordimeform

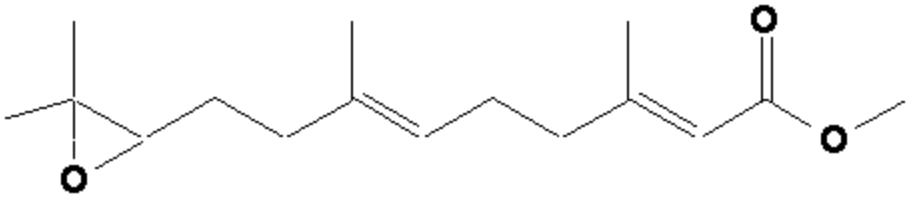


Tremors, convulsions, death

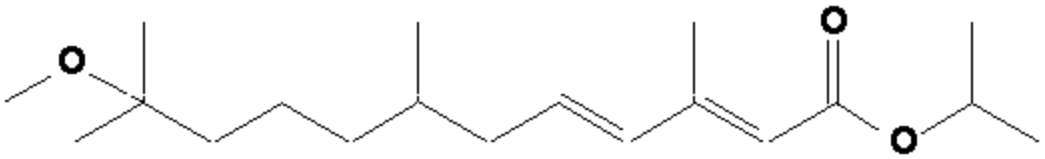
JH mimics (analogues)

Prevent metamorphosis and adulthood

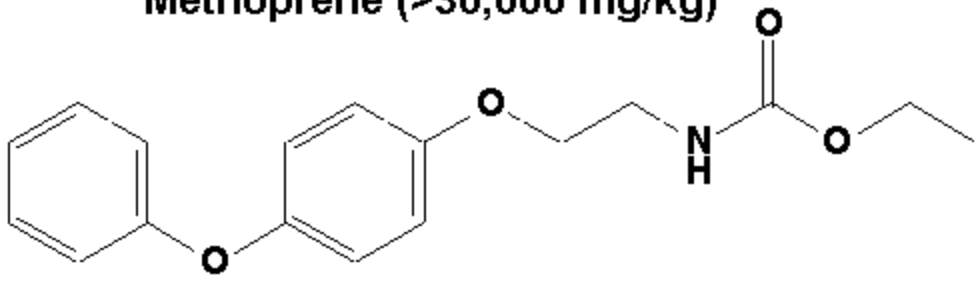
Inhibit reproduction



Juvenile Hormone III

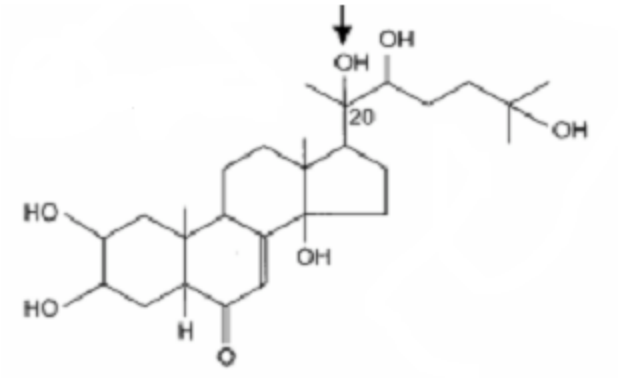


Methoprene (>30,000 mg/kg)

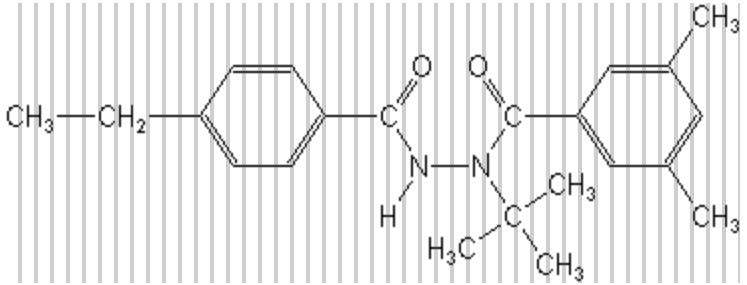


Fenoxycarb (16,800 mg/kg)

Ecdysone mimics

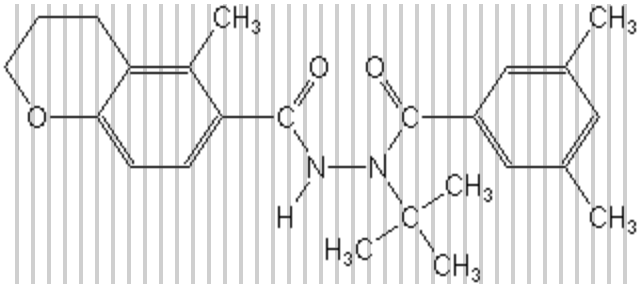


20-hydroxyecdysone



Tebufenozide

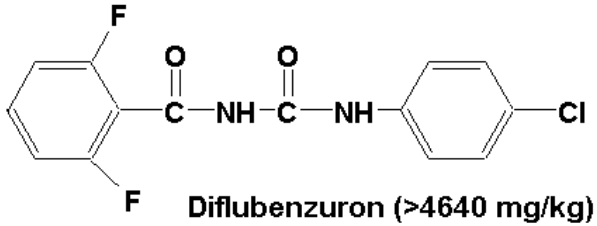
- Mimic actions of molting hormone and cause premature molt
- Insects stop feeding
- Soft on non-target organism
- Slow



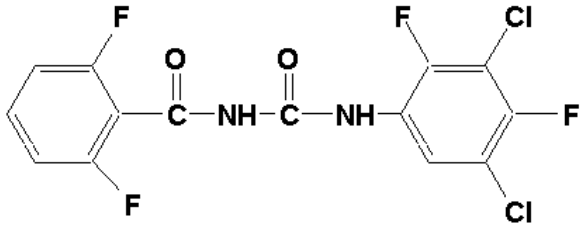
Chromafenozide

Chintin systhesis inhibitors: BPU

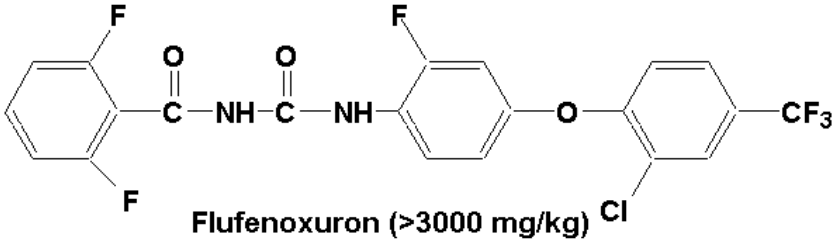
- BPU= Benzoylphenyl Urea
- Inhibit chitin syntheses, larvae died during molting
- Insect growth regulator (IGR): BPU, JH analogues and molting hormone mimics disrupt normal growth and development of insects, thus collectively called IGR



Diflubenzuron (>4640 mg/kg)



Teflubenzuron (>5000 mg/kg)



Flufenoxuron (>3000 mg/kg)

Mode of action=target site

- Neurotoxins: Nerve system
  - Voltage-gated Na+ channel modulators: DDT and Pyrethroids
  - Acetylcholine receptor (AchR) agonist: Neonicontinoids and Spinosad
  - Acetylcholine esterase (AchE) inhibitors: OP (organophosphates) and Carb (carbamates)
  - GABA-gated chloride channel agonist: Avermectin
  - GABA-gated chloride channel antagonist: cyclodienes of organochlorines and fipronil
  - Octopamine receptor agonist: Formamidines (chlordimeform and amitraz)
- IGR (Insect Growth Regulator)
  - Chitin synthesis inhibitors: Benzoylphenyl Urea
  - Endocrine system
    - JH analogues (JHA): methoprene, pyriproxyfen
    - MH analogues (MHA): tebufenozide, methoxyfenozide