

# Nitric Oxide and Lipid Peroxidation

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# Nitric Oxide is a Free Radical



⇒ Nitric oxide is not particularly oxidizing.  
Nitric oxide is (infinitely) stable\*.  
Nitric oxide does not rapidly react with organic  
molecules.

\*In the absence of dioxygen.

# The Nitric Oxide 'Radical' and some of its stable end-products

$\cdot\text{N}=\text{O}$  . . . nitric oxide

$-\text{O}-\text{N}=\text{O}$  . . . nitrite

$\text{RO}-\text{N}=\text{O}$  . . . alkyl nitrite

$\text{RS}-\text{N}=\text{O}$  . . . nitrosothiol

# Reactions of $\cdot\text{NO}$ with Other Free Radicals

Oxidation of  $\cdot\text{NO}$  to nitrite:



Nitric oxide reaction with organic peroxy radicals:

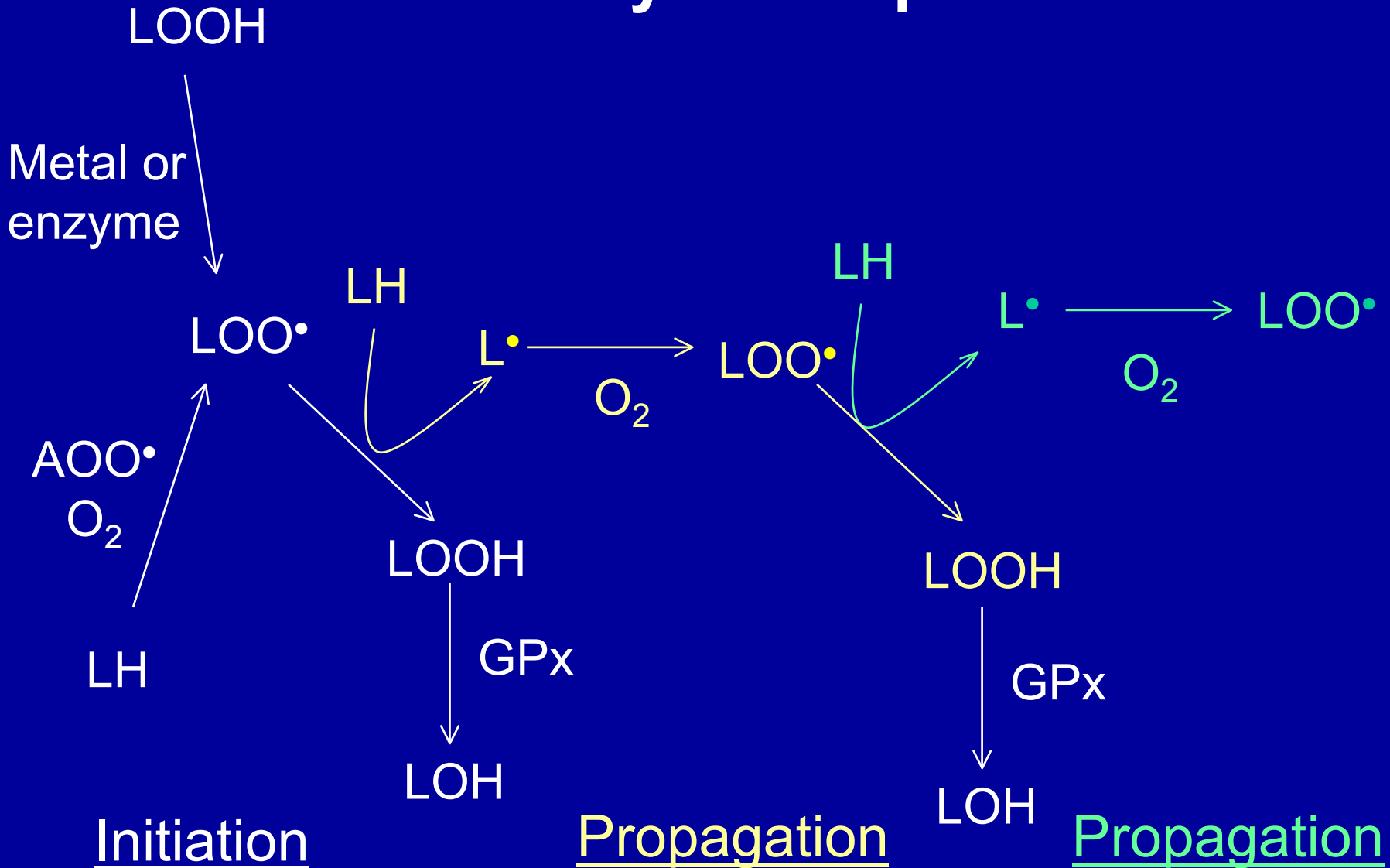


# Lipid Peroxidation

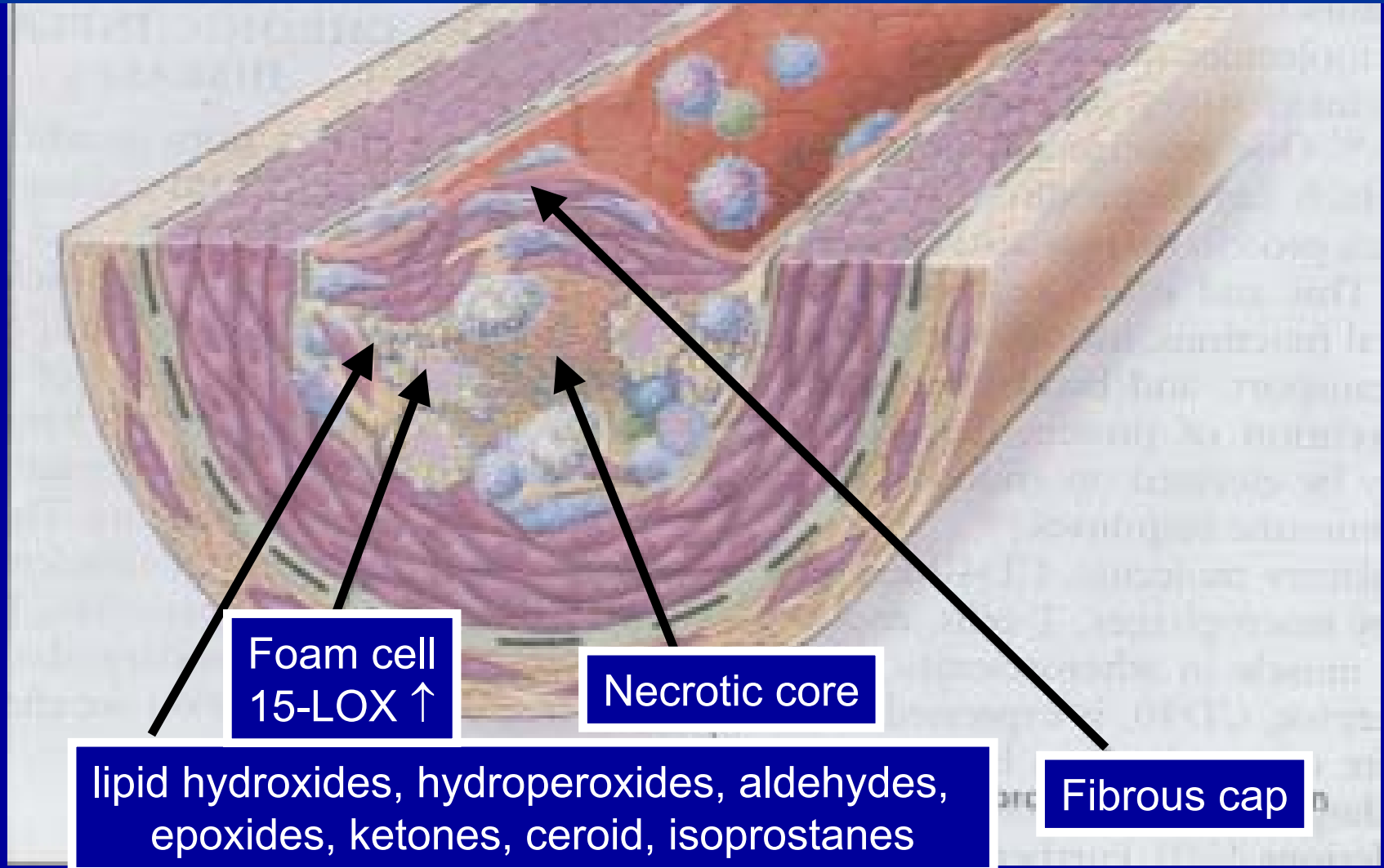


$\text{LOO}^\bullet$  is the central and rate-limiting species  
of lipid peroxidation

# Non-enzymatic lipid oxidation



# Lipid peroxidation products in an atherosclerotic lesion are both enzymatically and non-enzymatically produced.

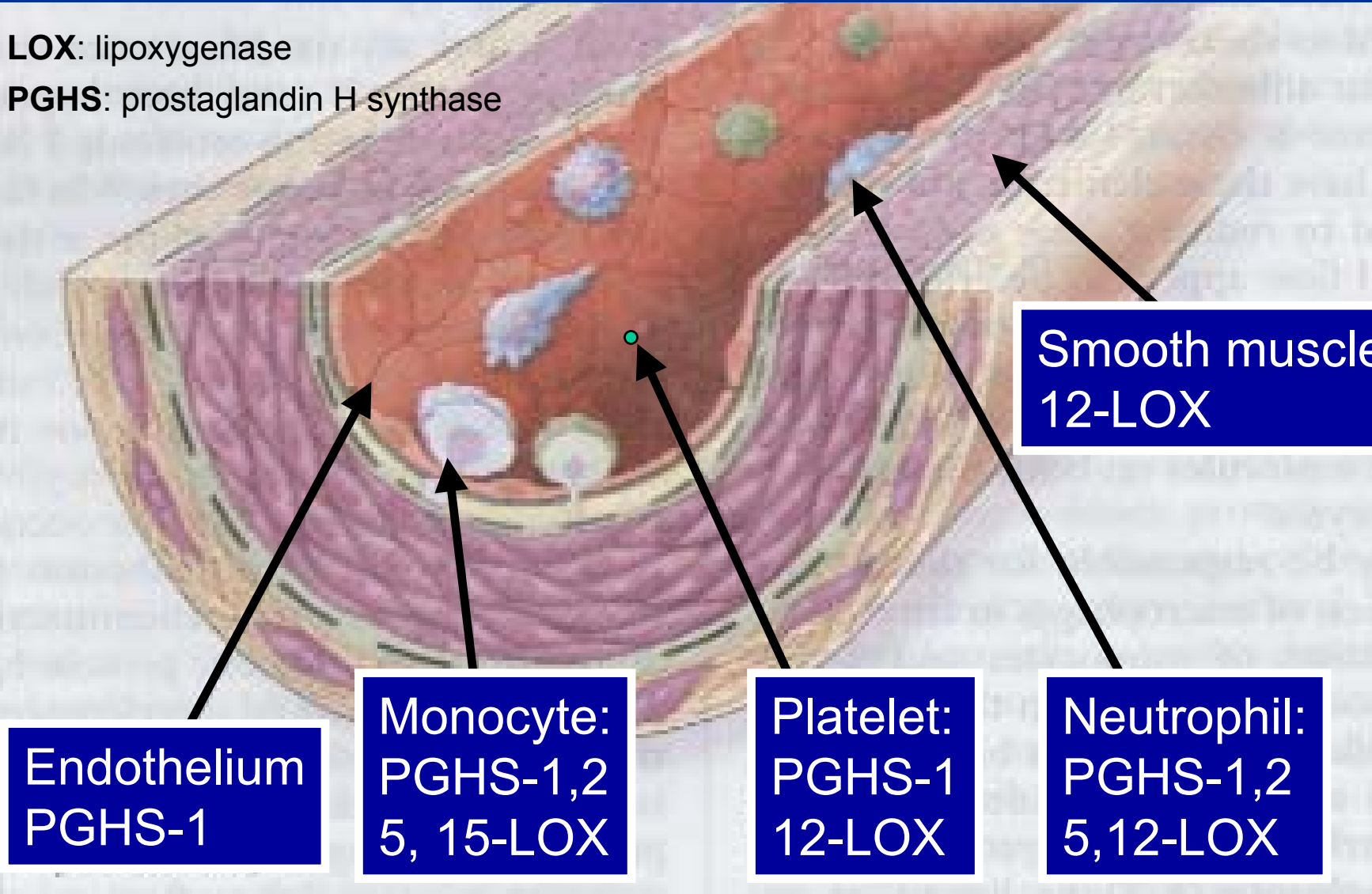




# Location of lipid oxidation enzymes in the vasculature

**LOX:** lipoxygenase

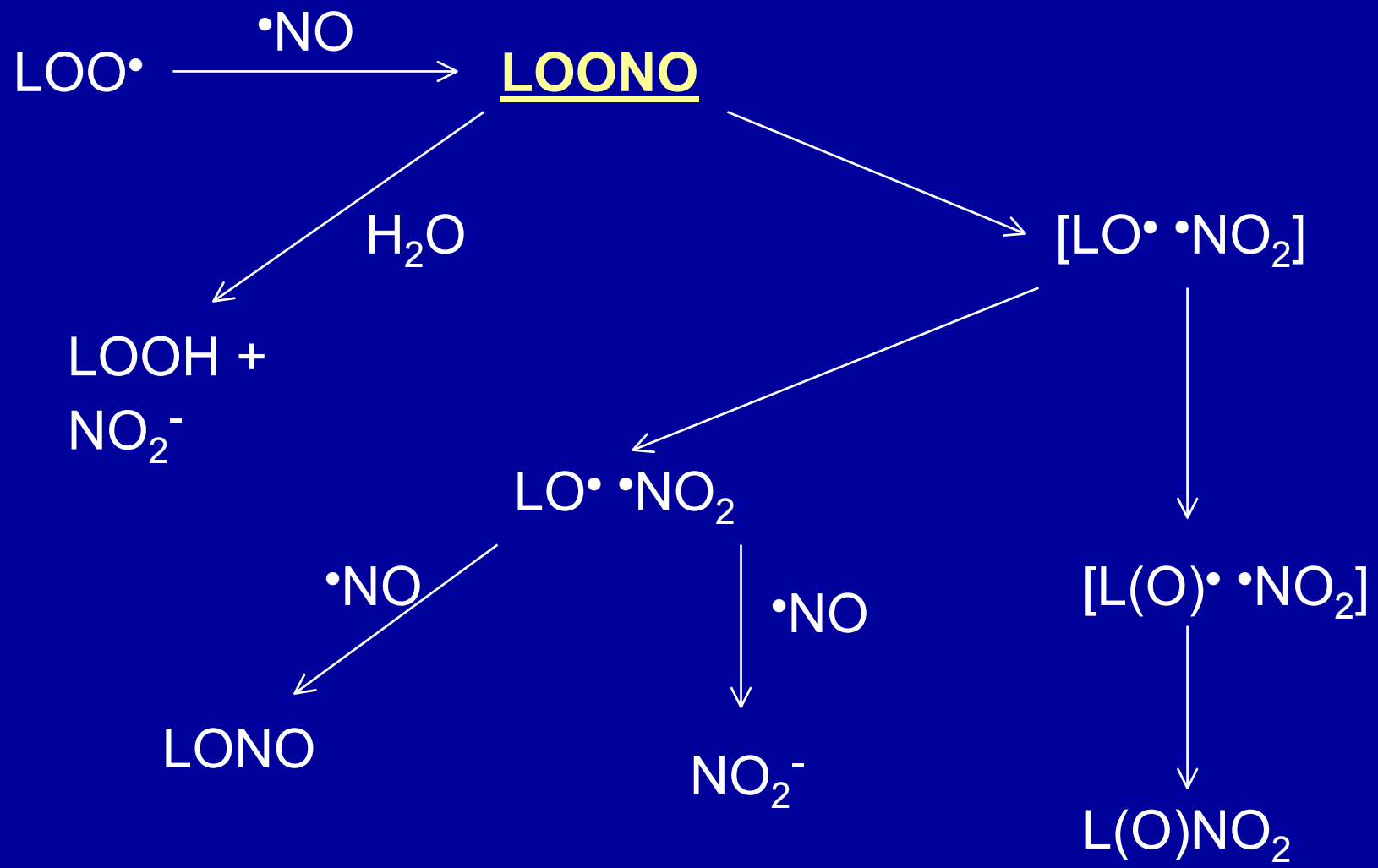
**PGHS:** prostaglandin H synthase



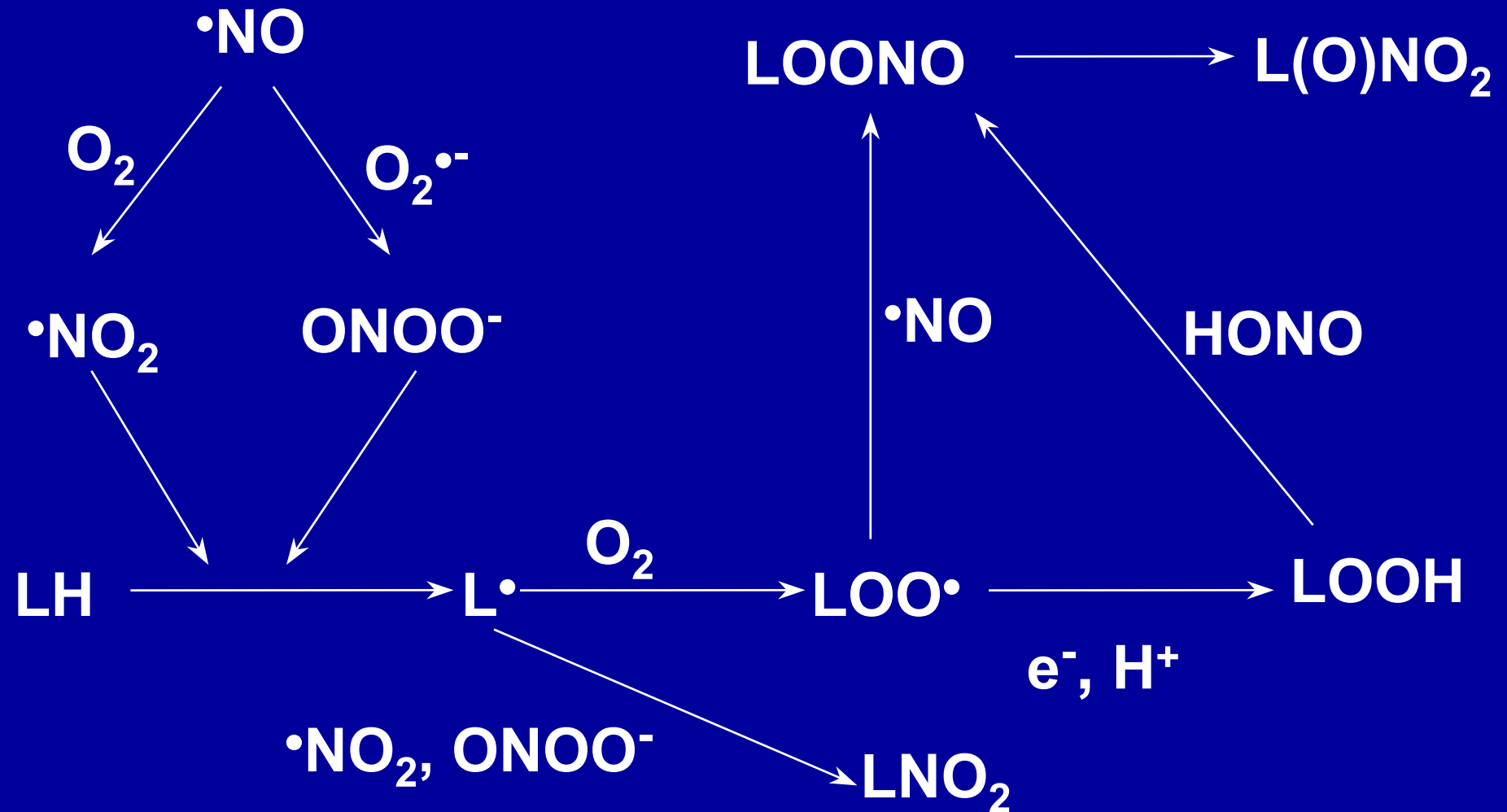
# Lipid oxidation enzymes are upregulated during vascular disease.

- \* Inhibition of 12-LOX restores blood pressure in Angiotensin-II dependent hypertensive rats.
- \* Increased products of PGHS in hypertensive rats, and PGHS inhibition restores blood pressure in humans and rats.
- \* Smooth muscle 12-LOX  $\uparrow$  in hypertension
- \* Platelet 12-LOX  $\uparrow$  in hypertension
- \* Foam cell/macrophage 15-LOX  $\uparrow$  in atherosclerosis.

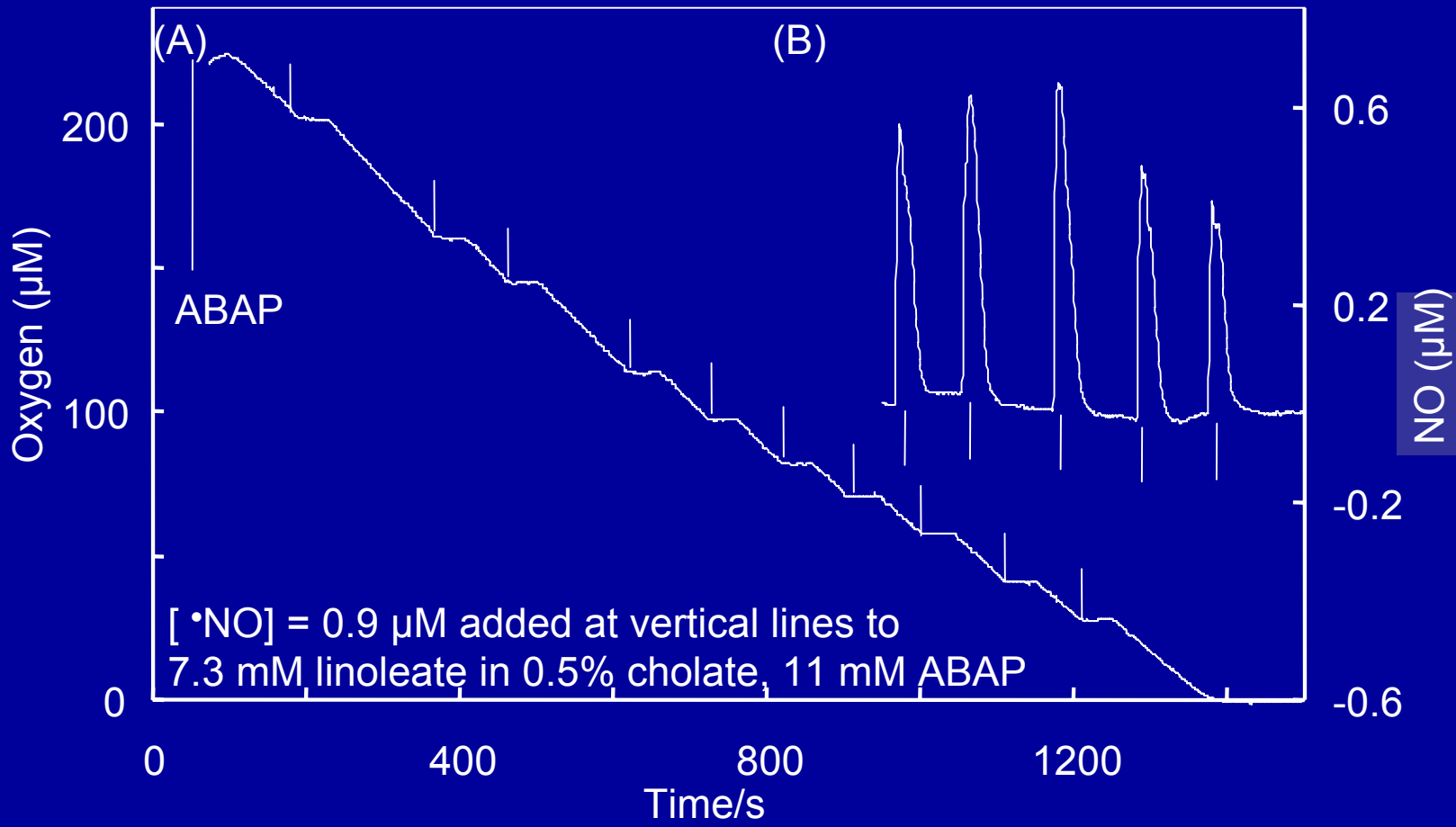
# Nitric oxide reaction with lipid peroxy radicals



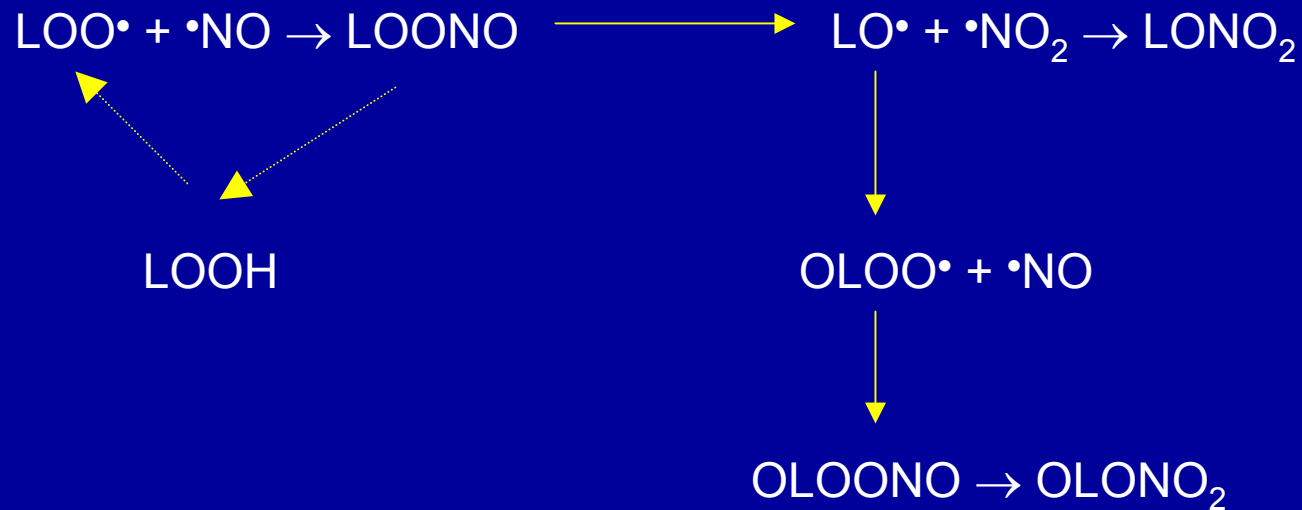
# Reactions between $\cdot\text{NO}$ -derived reactive nitrogen species and unsaturated lipid



# Nitric oxide inhibition of lipid oxidation coincides with fast rates of $\bullet\text{NO}$ uptake during ABAP-dependent linoleate oxidation.

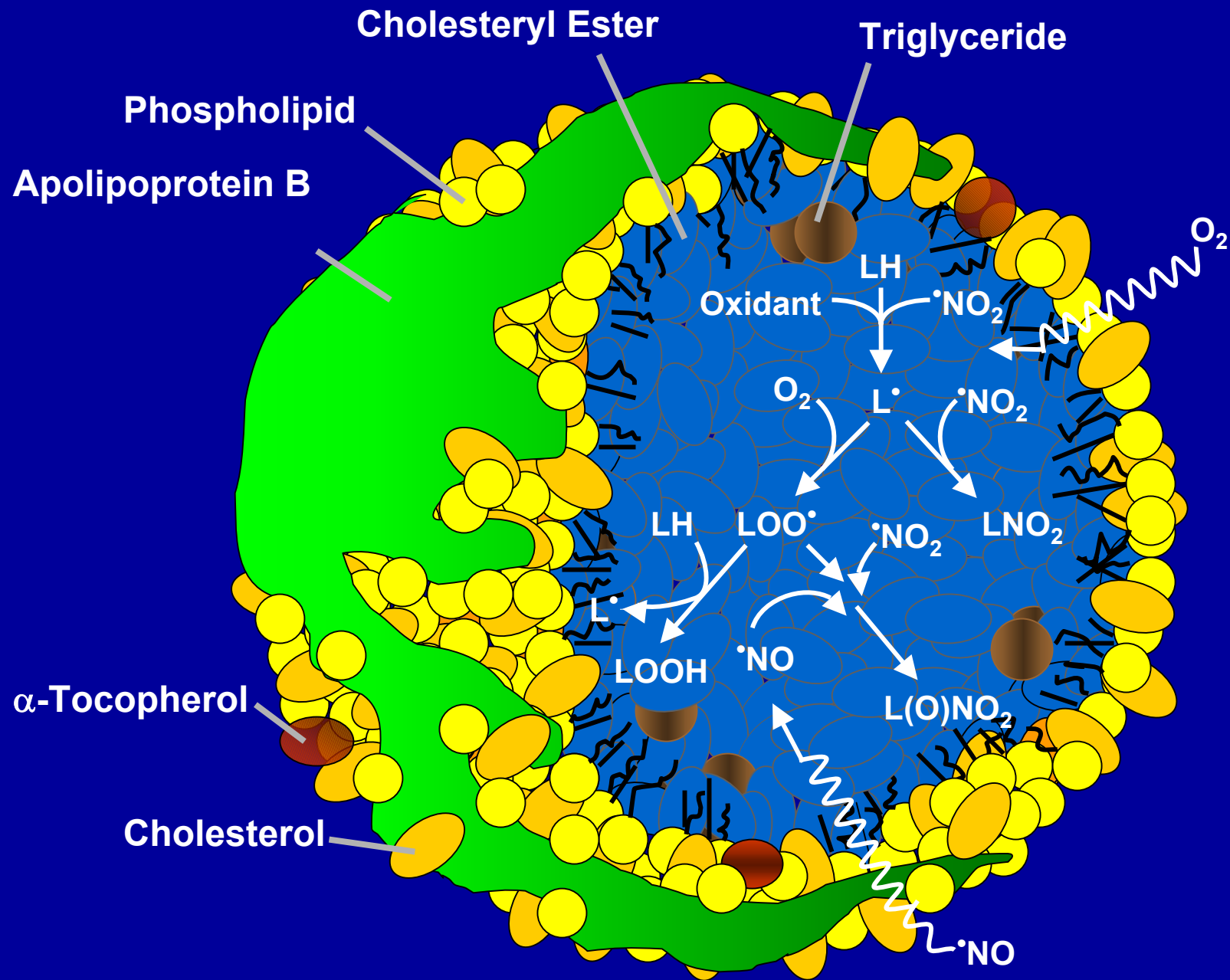


# Mechanism of Inhibition of LDL Oxidation by $\bullet\text{NO}$



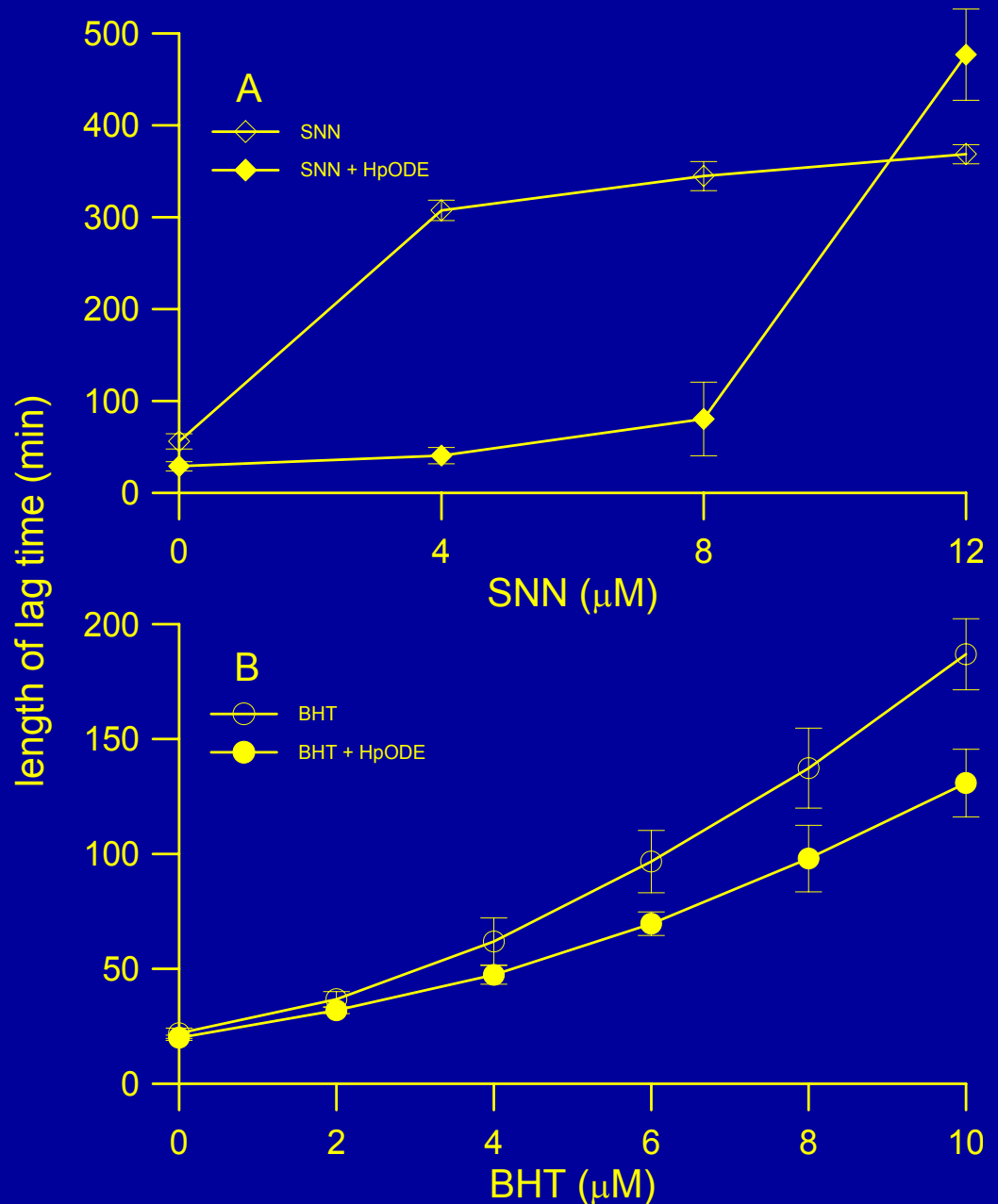
Two  $\bullet\text{NO}$  consumed for each  $\text{LOO}\bullet$





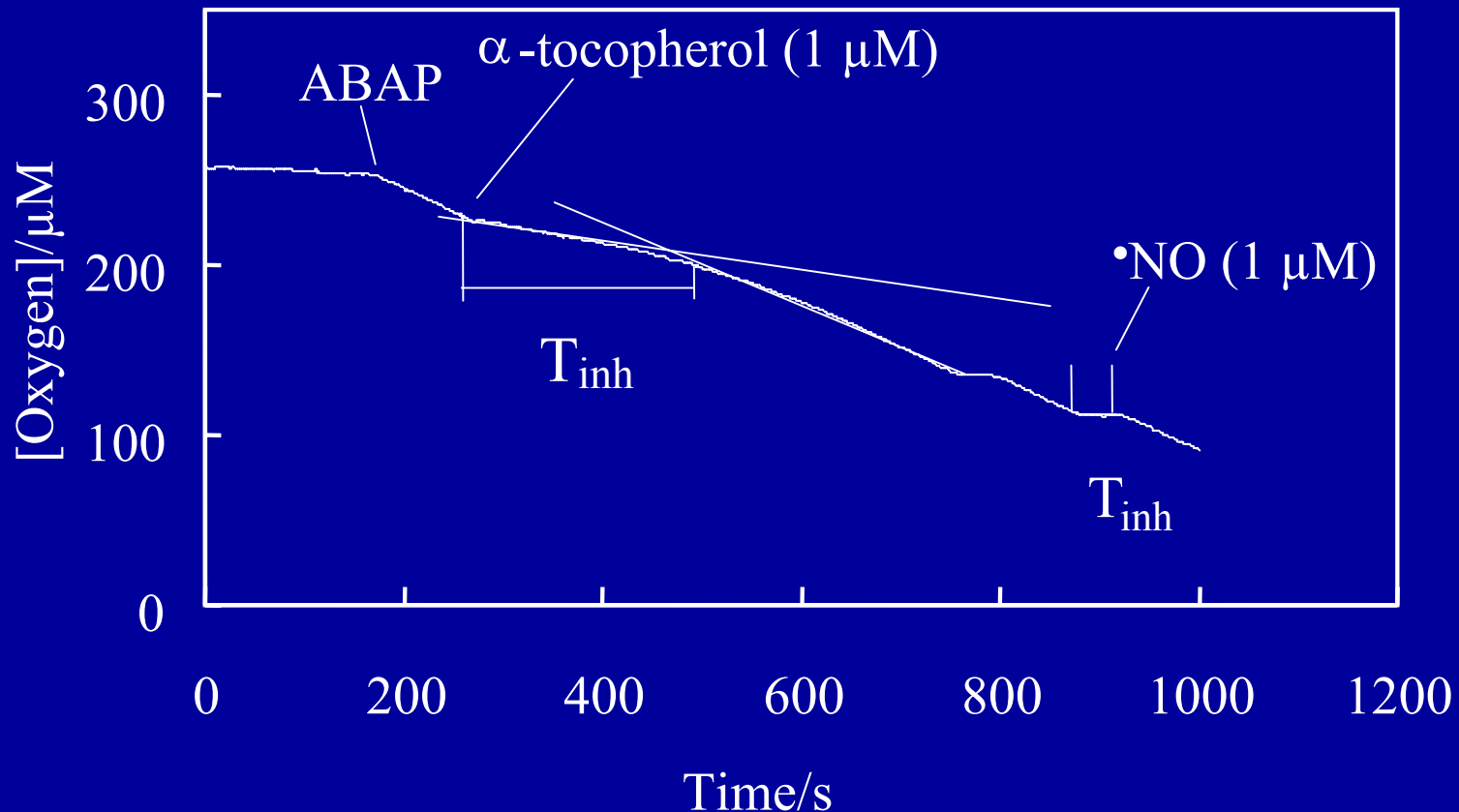
•NO and LDL Oxidation: The effect of HPODE

Lag time of LDL (125  $\mu\text{g/ml}$ ) oxidation by Cu(II) (20  $\mu\text{M}$ ) with and without HPODE (5  $\mu\text{M}$ )



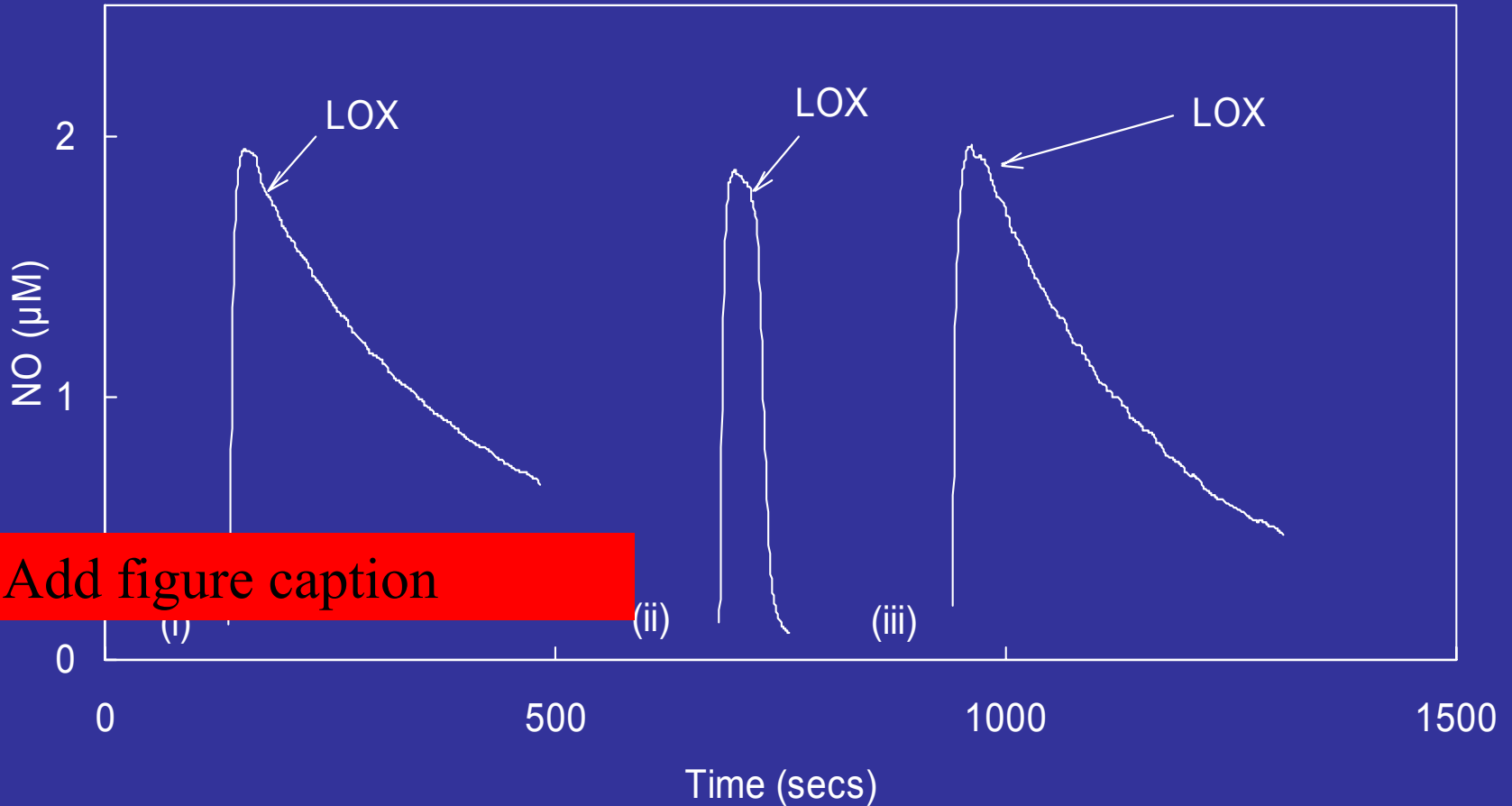


# Comparison of nitric oxide and tocopherol inhibition of linoleate oxidation.



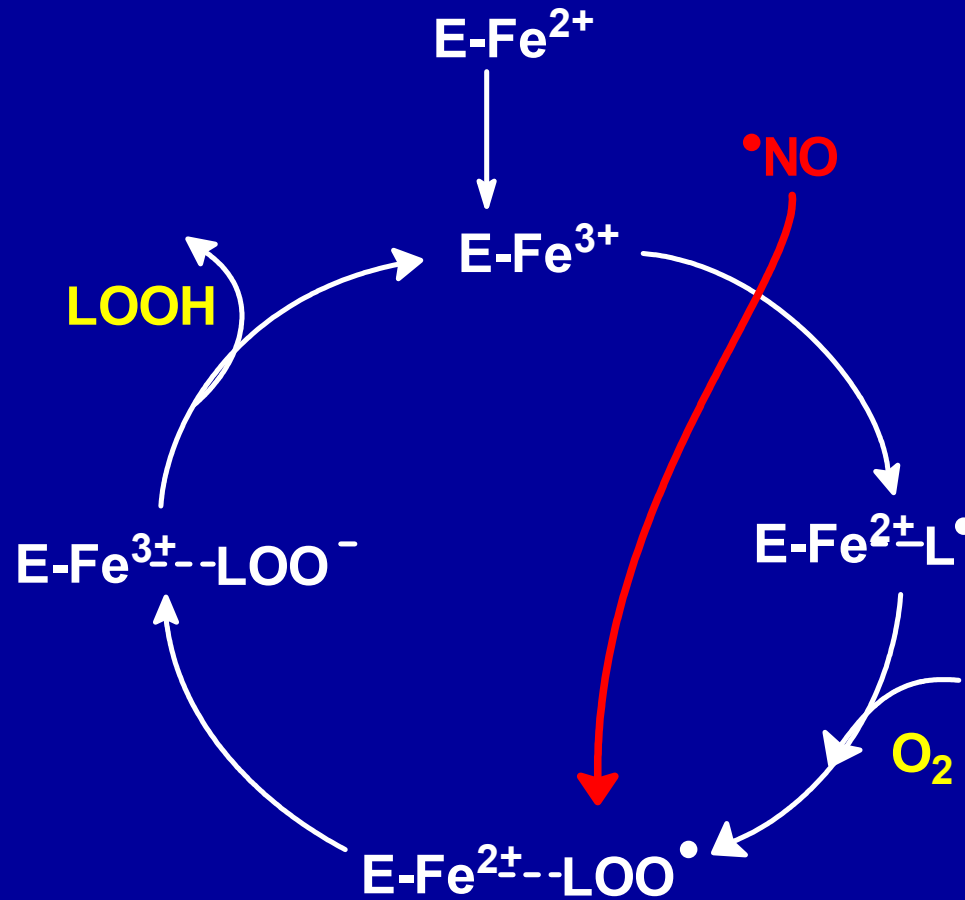
**Oxidation of linoleate (7.3 mM) by ABAP (11 mM)**

# Nitric oxide is consumed by rabbit 15-lipoxygenase during oxidation of linoleate.

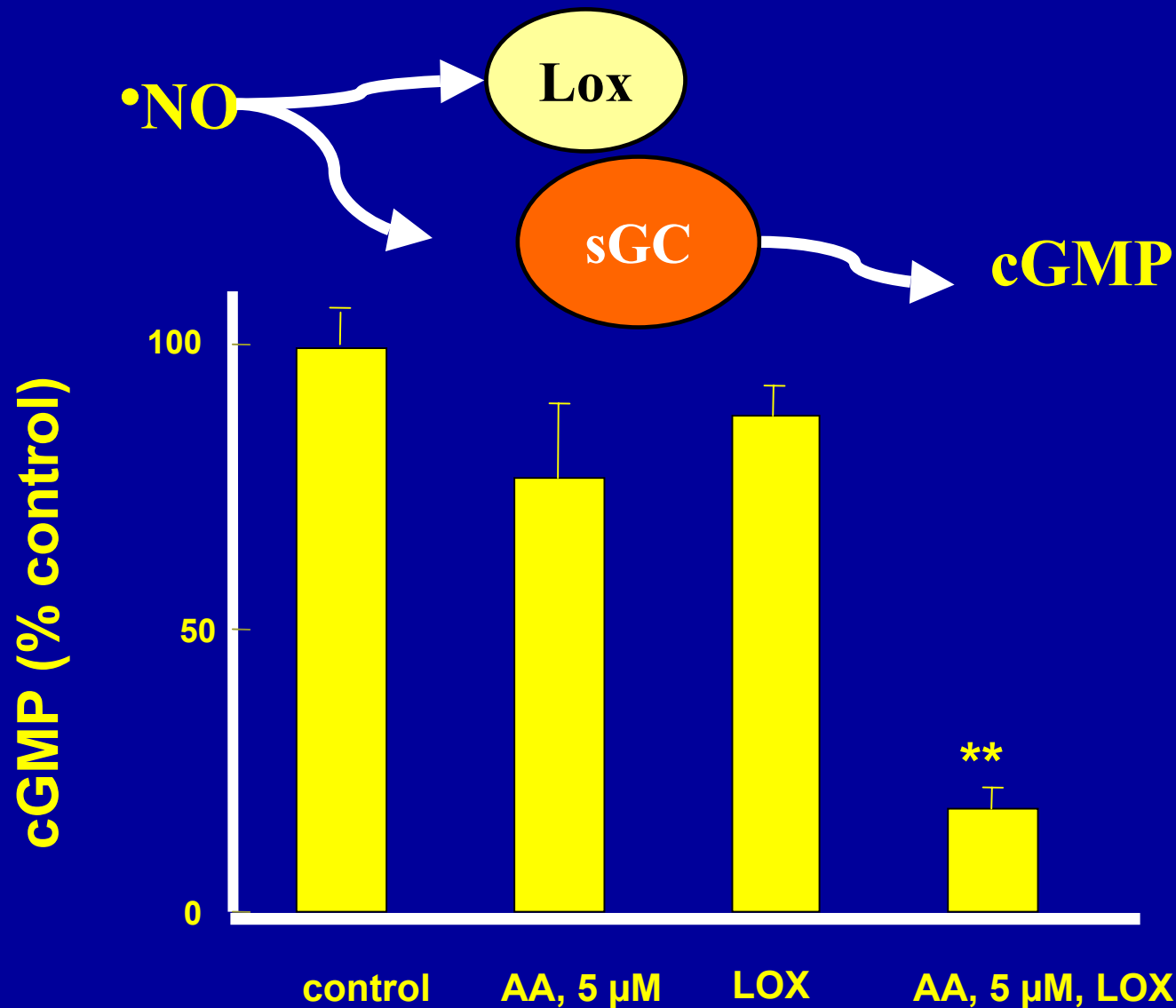


Add figure caption

# Site of lipoxygenase inhibition by $\bullet\text{NO}$



# Activation of LOX inhibits activation of sGC by $\bullet\text{NO}$



## Further Reading:

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