Isoprenoids

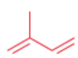
What are isoprenoids? (also called terpenoids)

Definition: ***hydrocarbons** structurally based on multiple isoprene unit*s

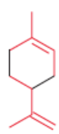
Introduction:

- names: 5C isoprene derivation = terpenoids (like "turpentine")
- huge structural diversity (20,000 structures), largest group of secondary plant metabolites
- exist mostly as multiples of **5 carbons units** (the Lego principle)
- types: **hemi**, **mono**-, **sesqui**-, **di**-, **tri**-, **tetra**-**terpenes** (5, 10, 15, 20, 30, 40 carbons)
  also polyterpenes (very large)
- two complementary biosynthetic routes are known, specialized for different groups of isoprenoids
  i) **mevalonate** (MVA) pathway
  ii) **deoxyxylulose phosphate** pathway

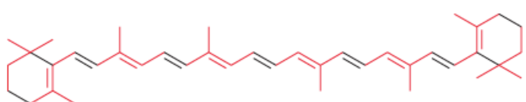
- impressive **functional diversity**: many **volatile** compounds, signals, toxins, hormones and more.
- some compounds form this family function as primary metabolites, but most fall into the secondary metabolite category
- many human uses of isoprenoids from or in plants (fragrances, flavors, pharmaceuticals, rubber)



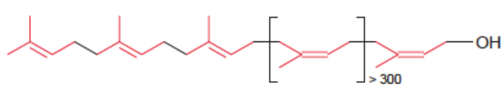
Isoprene



Limonene, a monoterpene



β-Carotene, a tetraterpene



Rubber, a polyterpene

Strategy and Outline

- learn basic biosynthesis pathways of isoprenoid building blocks.
- examples with specific functions of each class of isoprenoids

Overview of isoprenoid synthesis

Step 1: produce building isopentenyl (IPP) blocks (two pathways are possible)

I. Mevalonic acid (MVA) pathway:

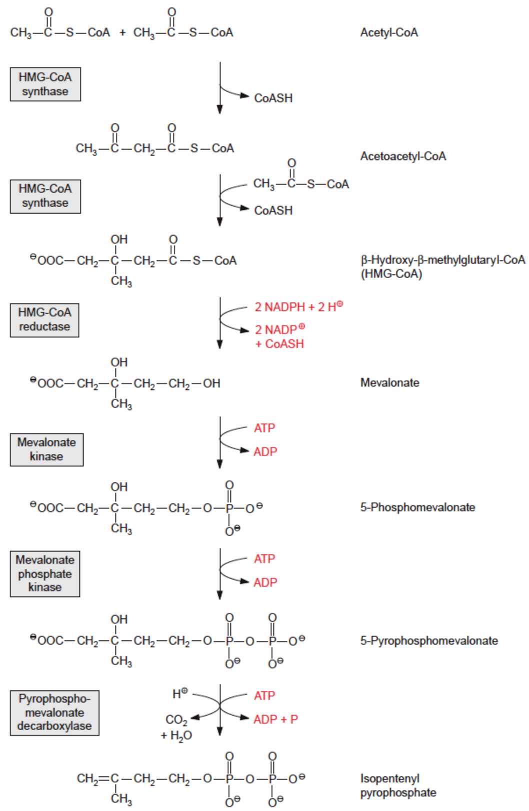
- **cytosolic** pathway (also found in animals - necessary for sterols and steroid hormones in vertebrates)
- leads to sesqui- and tri-terpenes, but typically not for the other terpene classes

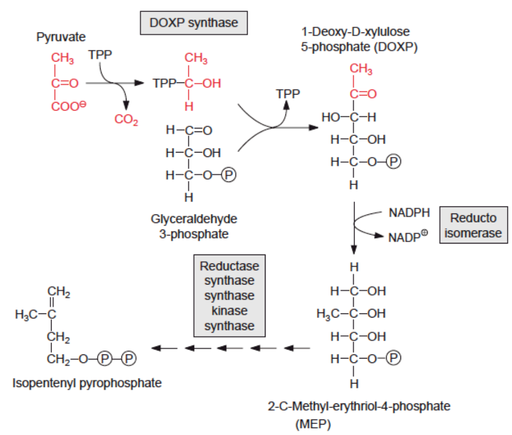
3x **acetyl-CoA** --> --> **mevalonic acid** (6C) --> --> isopentenyl pyrophosphate (IPP) <--> dimethylallyl pyrophosphate (DMAPP)

Key enzyme: *Hydroxymethylglutaryl CoA (HMGCoA) synthase* (key gateway enzyme)

Also: - hydroxymethylglutaryl CoA (HMGCoA) reductase

- kinases, dehydratases, & IPP isomerase





II. Deoxyxylulose phosphate (**DXP**) pathway

- in **plastids**, mostly independent of MVA pathway (little exchange)
- leads to <u>mono</u>-, <u>di</u>-, and <u>tetra</u>-terpenes
- also found in bacteria, some protists, algae

Precursors: **pyruvate** & **glyceraldehyde-3-P**

- products: both IPP and DMAPP
- key enzyme: *deoxyxylulose phosphate (DXP) synthase*

<u>Step 2: Successive condensations of IPP and DMAPP</u>

- head-to-tail ('lego')
- enzymes: *prenyl transferases:*

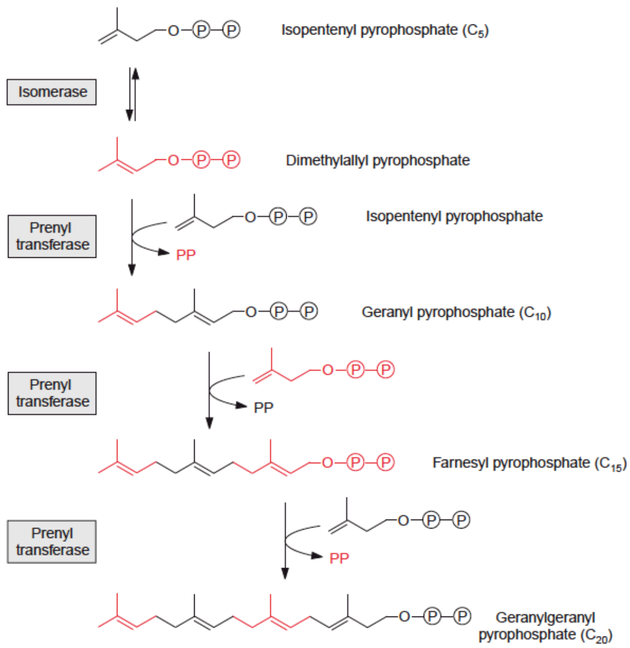
1 IPP + 1 DMAPP --> **geranyl-PP** (to monoterpenes)

geranyl-PP synthase

2 IPP + 1 DMAPP --> **farnesyl-PP** (to sesquiterpenes)

farnesyl-PP synthase (one enzyme)

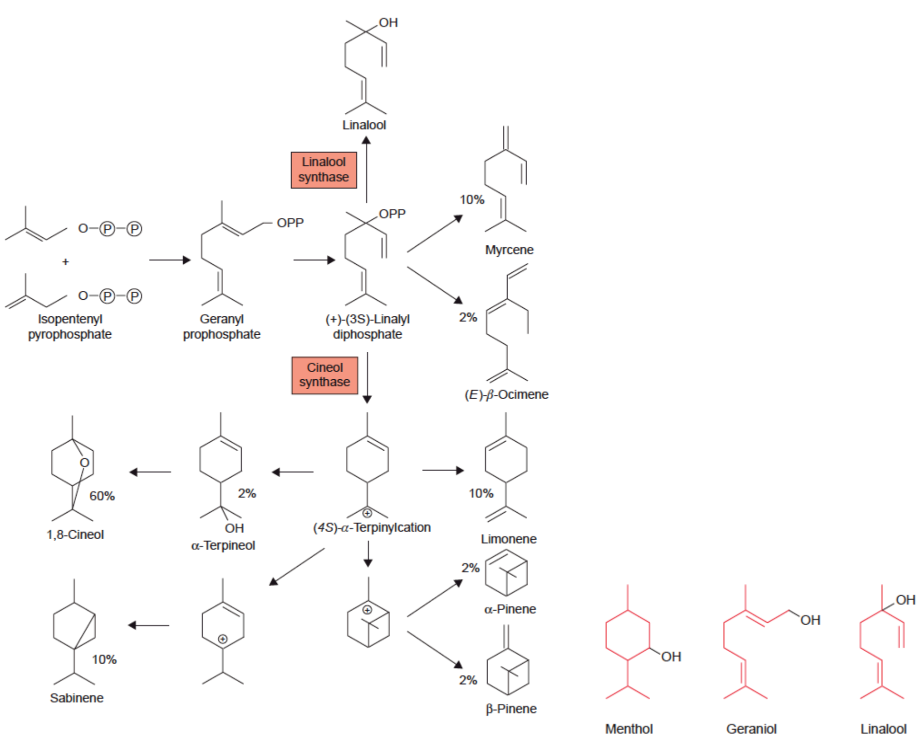
3 IPP + 1 DMAPP --> **geranylgeranyl-PP** (to diterpenes)
geranylgeranyl-PP synthase (one enzyme)



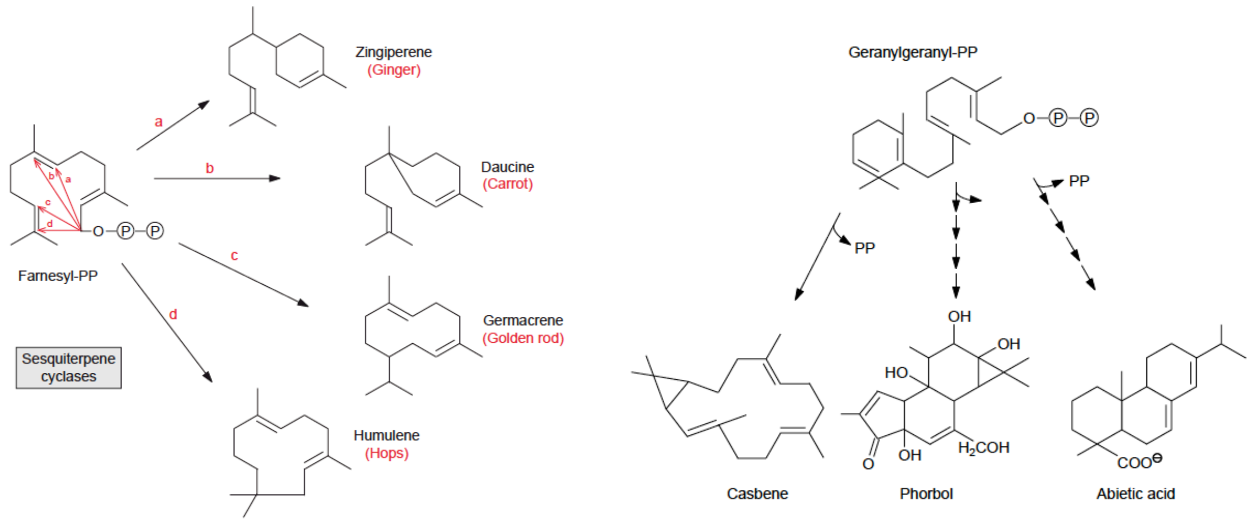
Step 3: Further elaborations & modifications

- cyclizations (*terpene synthases - TPSs*)
  - one enzyme specifies product types: mono-, -sesqui, di-terpenes, (but may produce several products)
  - secondary modifications: hydroxylations, oxidations, reductions, carbon skeleton rearrangements

Example monoterpene synthases: **linalool synthase** (specific), **cineol synthase** ('sloppy')



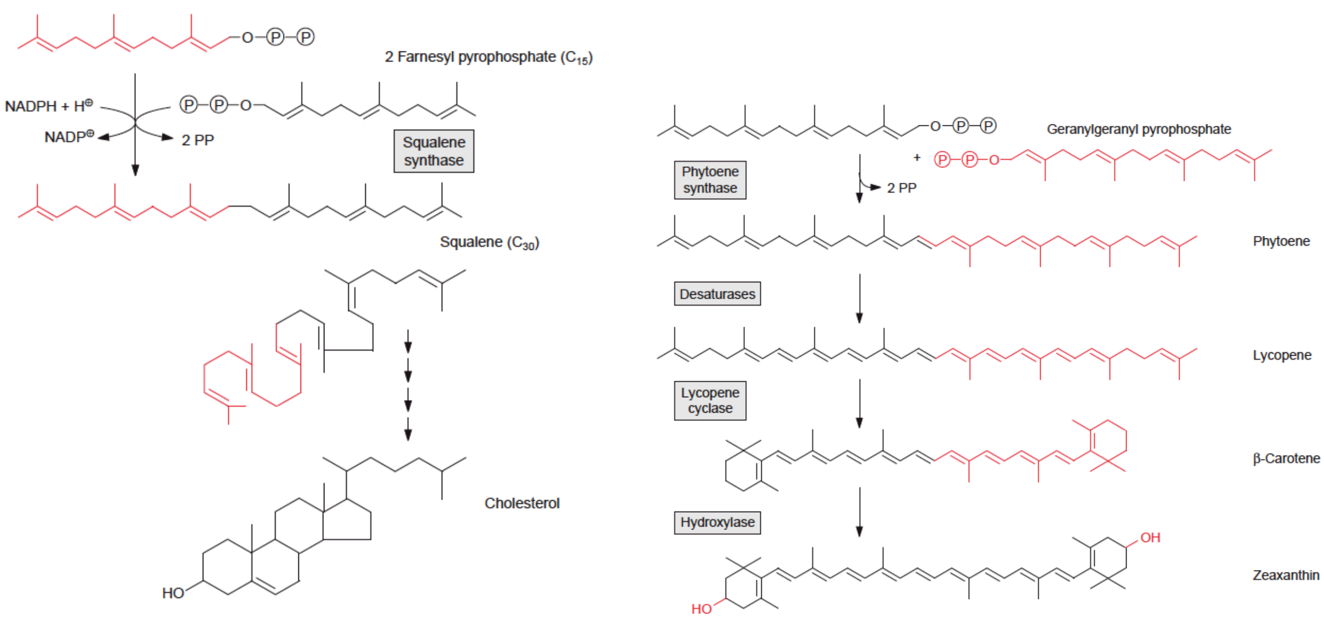
Example: sesquiterpene synthases, diterpene synthase



Step 4. Further condensations to tri- and tetra-terpenes

2 x farnesyl-PP --> triterpenes (sterols and steroids, cardiac glycosides, others)
enzyme: squalene synthase

2 x geranylgeranyl-PP --> tetraterpenes (carotenoids, xanthophylls and derived products
enzyme: phytoene synthase



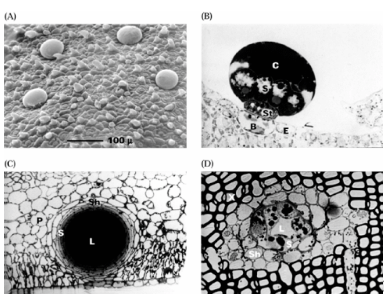
Isoprenoid functions in plants (some examples)

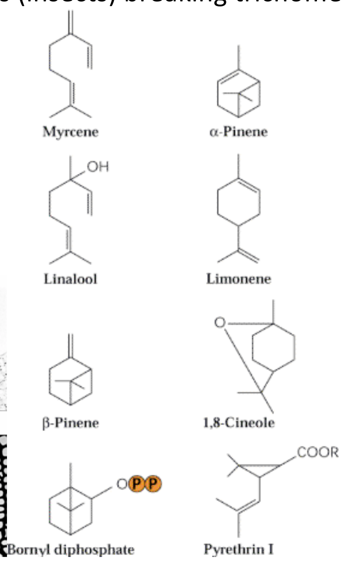
1. Hemiterpenes (volatile):
- isoprene released from leaves (from DMAPP)
- greenhouse gas from forests (blue mountains)
- up to 15 % of fixed carbon - why? heat stress?

2. Functions for monoterpenes and sesquiterpenes

i) some are **direct defenses** (toxic/repellent)

Example: peppermint trichomes (special modified hairs) contain monoterpenes and sesquiterpenes
- released by herbivores (insects) breaking trichome





ii) MTs are solvents for **oleoresin** (see diterpene acids)

iii) Many mono- or sequiterpenes are **volatile** (= ***ecological signals***)

Example: attract pollinators, seed dispersors (see scents and fragrances

(eg) linalool, limonene (recall: methyl benzoate, a phenolic volatile)

- attract predators (=act as **indirect defenses**)

i) *C. nigriceps* (parasitic wasp) is very efficient in finding tobacco budworm (*H. virescens* = host)

→ find damaged plants even if caterpillar larvae have been removed)

→ differentiate between *H. virescens* (***host***) vs *H. zea (**nonhost**)*

ii) damaged leaves release volatile isoprenoids

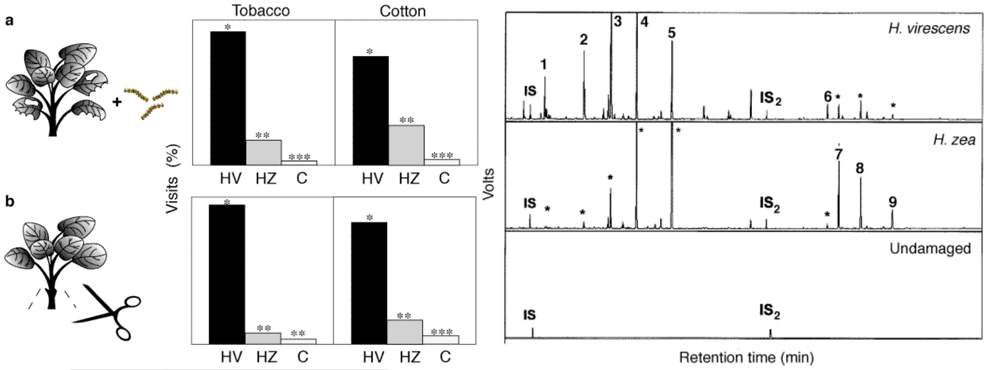
→ differences in volatiles differentiat **host** and **non-host** plants

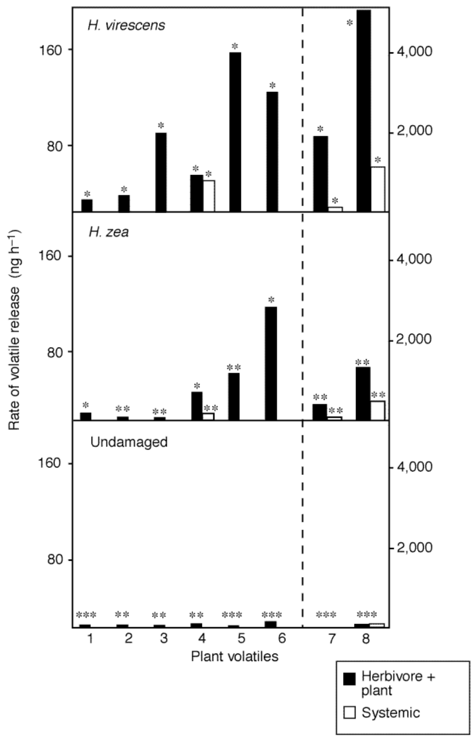
→ systemic leaves: undamaged leaves on damaged plants

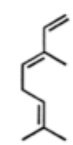
iii) parasitic wasps detects the volatiles

iv) works with multiple species (tobacco, cotton, corn)

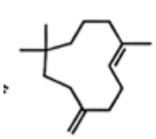
v) volatiles are stimulated by **volicitin,** a novel compound first found in caterpillar saliva



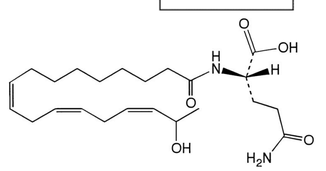




ocimene



caryophyllene



Volicitin

N-(17-hydroxylinolenoyl)-L-glutamine