In silico reconstruction of *Copaifera multijuga* Hayne terpenoids network

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Outline

Introduction
   Terpenoid metabolism
   Sesquiterpene cyclases
   Copaifera multijuga Hayne

Method

Preliminary results
Metabolism
Set of metabolic reactions and physicochemical processes occurring in a live organism.

- **Primary metabolism**
- **Secondary metabolism**
  - polyketides (PKS)
  - non-ribosomal peptides (NRP)
  - alkaloids
  - terpenoids
Terpenoids

- hydrocarbons resulting from the combination of several isoprene units
- interact as signal molecules for:
  - communication intra/inter species
  - attracting pollinating insects
- act as a defense against herbivores and microbes
- vast applicability in medicine and biotechnology
Terpenoid biosynthesis

Compartementalized biosynthesis of IPP and DMAPP [3].
Terpenoid biosynthesis

\[
\text{IPP} + \text{DMAPP} \rightarrow \text{Geranyl pyrophosphate (GPP)}
\]

\[
\text{IPP} + \text{Geranyl pyrophosphate (GPP)} \rightarrow \text{Farnesyl pyrophosphate (FPP)}
\]

\[
\text{Farnesyl pyrophosphate (FPP)} + \text{IPP} \rightarrow \text{Geranylgeranyl pyrophosphate (GGPP)}
\]
Cyclization mechanisms

- C – C bonds formation
- Cationic intermediates
- Hydride, methyl, and allyl shifts
- Wagner-Meerwein rearrangements
- Carbocation capture by water
Cyclization mechanisms

Initial cyclization mechanisms for sesquiterpenes biosynthesis [2] [1].
Sesquiterpene cyclases

- 500–580 amino acids
- aspartate-rich region, DDxxD
- often a second motif, NSE/DTE
- product specificity:
  - dependent on the amino acid residues, and
  - constraints of the active site
Cyclases classification
Copaifera multijuga Hayne

Area of occurrence of *Copaifera multijuga* Hayne in Brazil.
Copaifera multijuga Hayne

42 sesquiterpenes of *Copaifera multijuga Hayne*’s oil-resin.
Copaifera multijuga Hayne

Percent amount of sesquiterpenes in *C. multijuga* Hayne's oil-resin.
Method

For the 42 known sesquiterpenes of *Copaiba*:
- Can we confirm the literature reported cyclizations?
- Can we propose new predicted cyclizations?

For the transcriptome of *Copaiba*:
- Can we use a cyclization family based HMM profile to annotate the enzymes?
Method

- Identified cyclizations
- Graph rewrite rules
- HMM profiles
- Alignments

C. multijuga Hayne transcriptome

Known compounds
New compounds
Cyclases annotation
Cyclizations identified in the literature for *Copaifera multijuga Hayne* compounds.
Preliminary results

Unfiltred and filtered results for $\beta$-caryophyllene cyclization experiment.
Next steps

- Update 2Path database to a new level of details;

- Expand source sequences for the HMM profiles;

- Make available pathway searches from submitted sequences.

_A terpenoid metabolic network modelled as graph database_
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References

