Université de Lille

How do we deal with monomers in Norine ?

Norine: a database of nonribosomal peptides (NRPs)

What are nonribosomal peptides ?

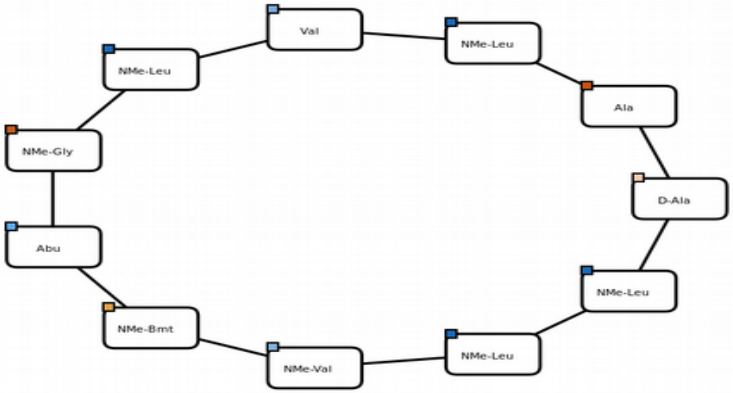
synthesized by huge enzymatic complexes

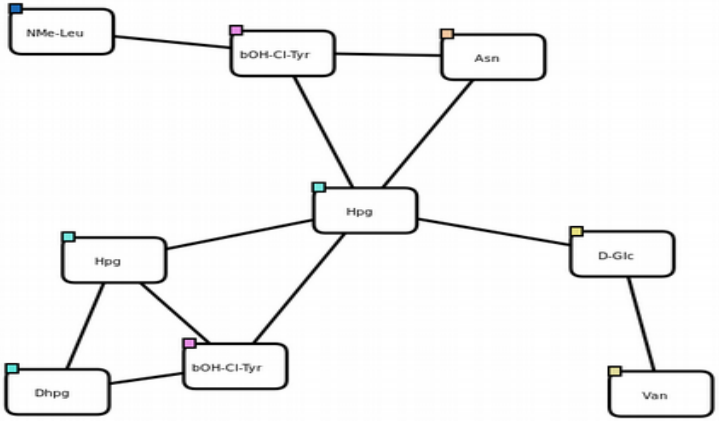
> 500 monomers

various 2D structures (cycles, branches)

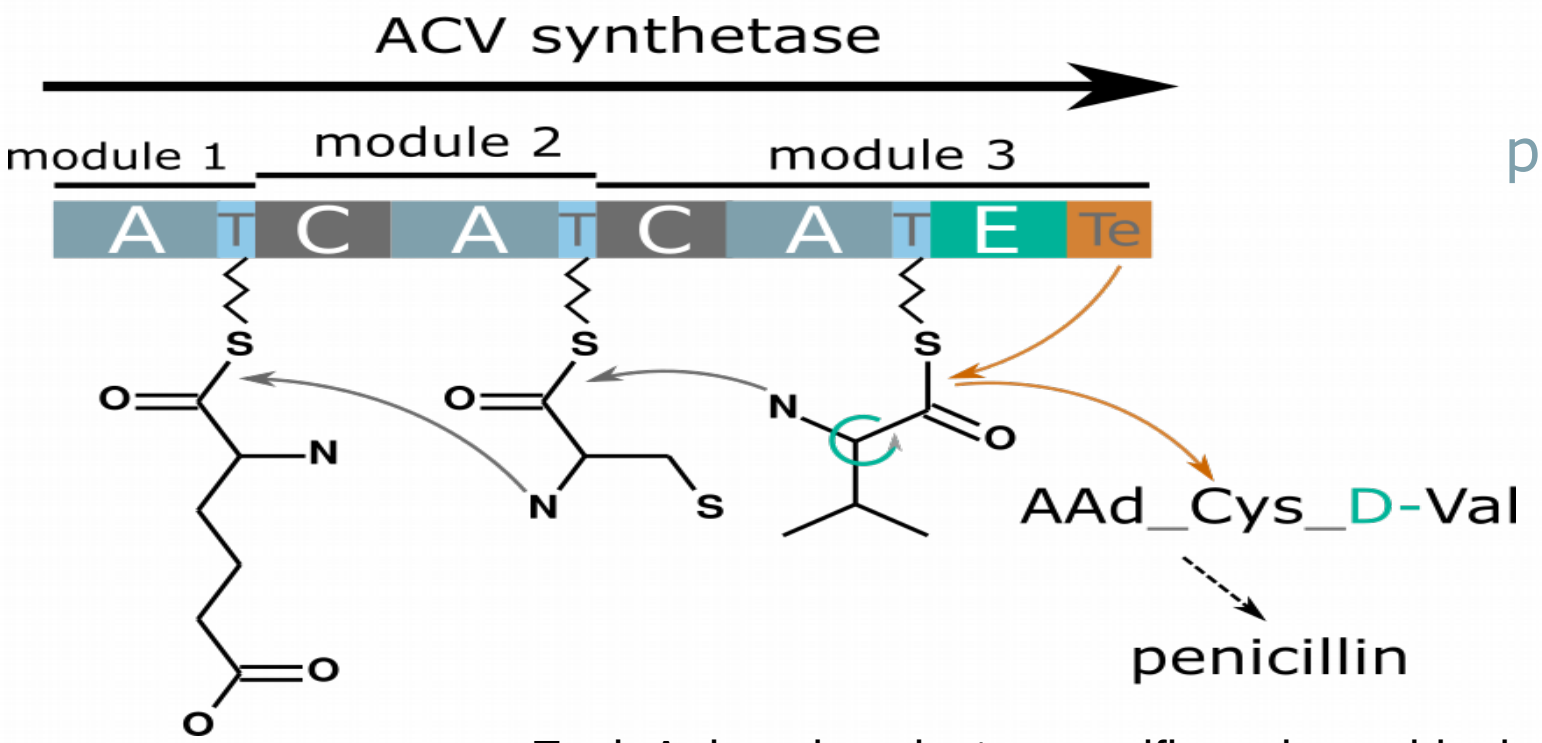
various interesting activities

synthesized by bacteria and unicellular fungi





NRP synthesis: huge specificity



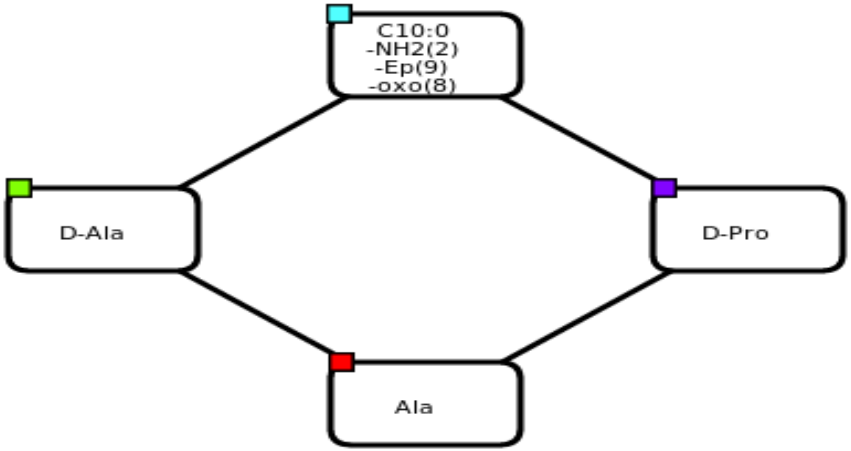
a given nonribosomal peptide synthetase

a specific nonribosomal peptide

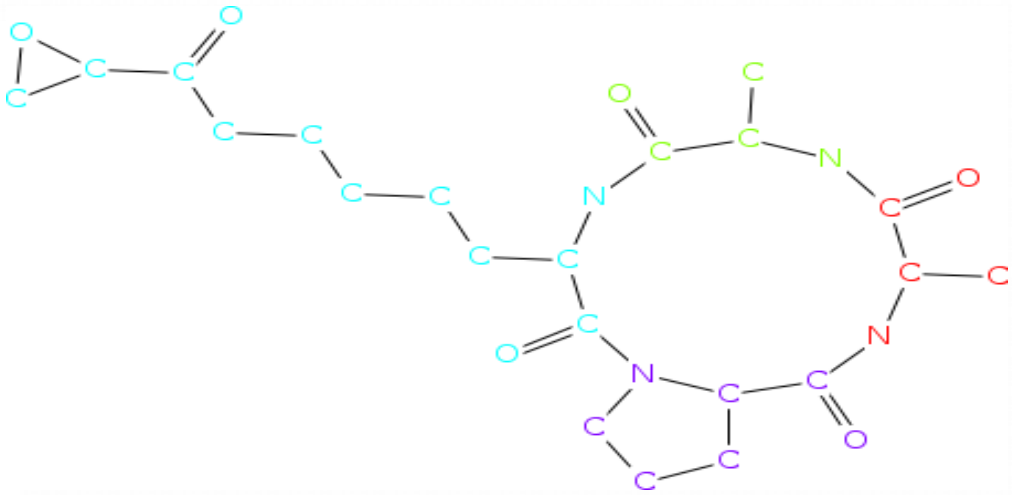
Each A domain select a specific amino acid, always the same

Norine: two structure representations for the NRPs

monomeric graph



atomic graph



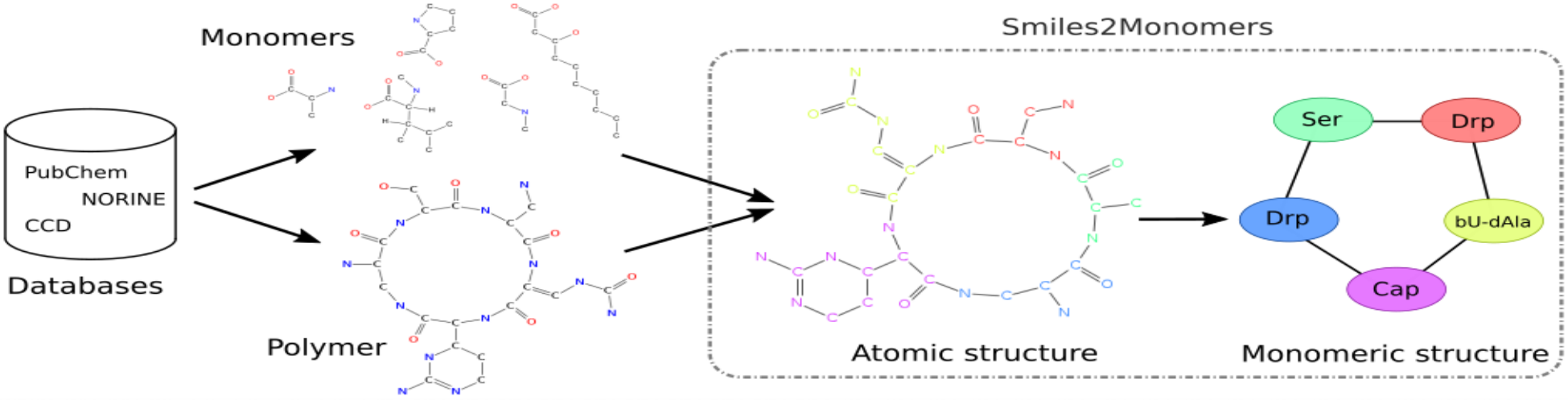
CC2NC(=O)C(C)NC(=O)C3CCCN3(C(=O)C(CCCCCC(=O)C1CO1)NC2(=O))

D-Pro,Ala,D-Ala,C10:0-NH2(2)-Ep(9)-oxo(8)@1,3@0,2@1,3@0,2

Norine: determination of the monomeric graph

- manual and visual fragmentation of chemical structures from articles
  - structures determined by mass spectrometry
  - study of the NRP synthesis with experiments to determine substrate specificity and bioinformatics analysis of the synthetases

- automatic determination with our tool : SMILES2monomers



Our comments and questions about what is a monomer ?

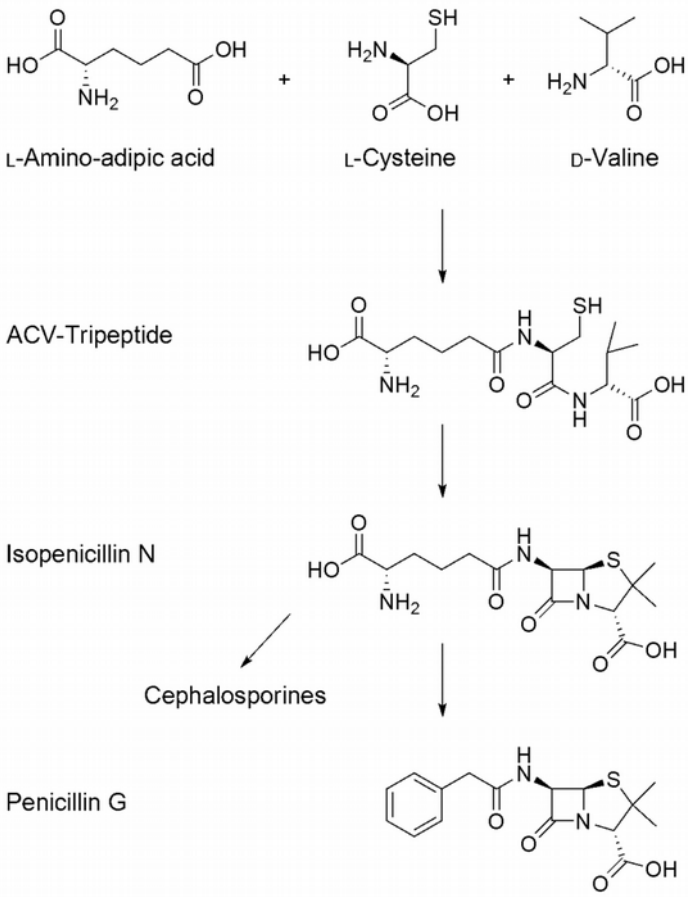
- NRPs synthesis is done by making bonds between monomers

  => monomer = compounds used by the enzyme to synthesize the NRPs

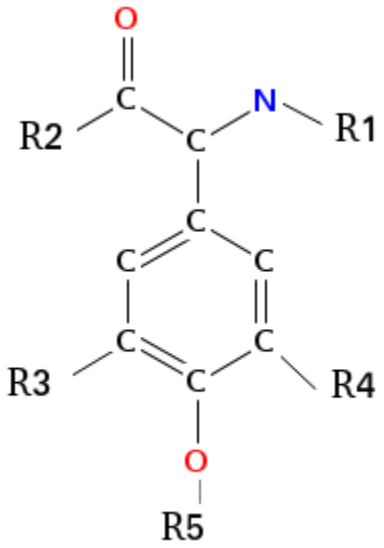
- **BUT** they can be modified during the synthesis
  - by optional domains in the synthetase
    - example : L → D forms, addition of Met, heterocyclisation
  - by external enzymes
    - example : formation of β-lactam, addition of carbohydrates

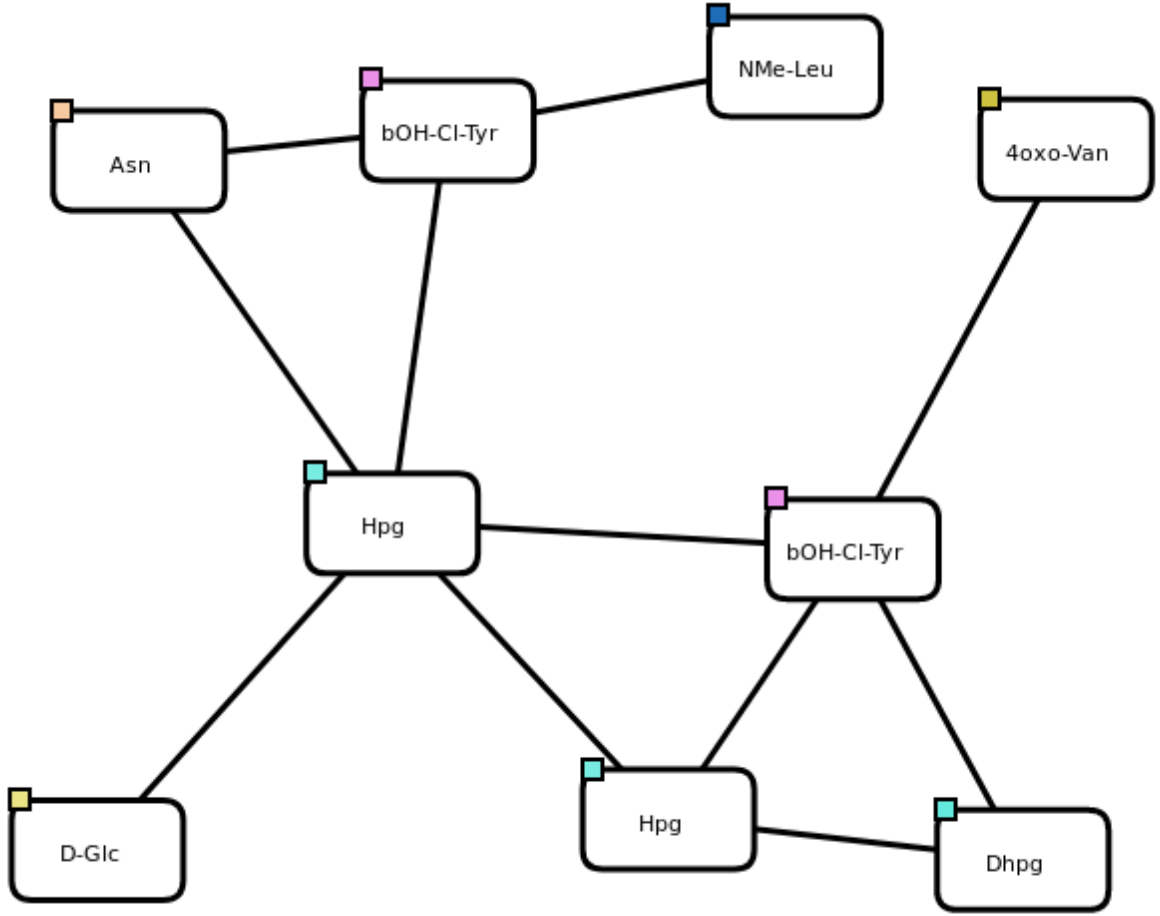
  => initial monomers are no more identifiable

  => automatic fragmentation is not applicable

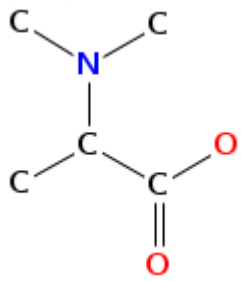


A complex peptide

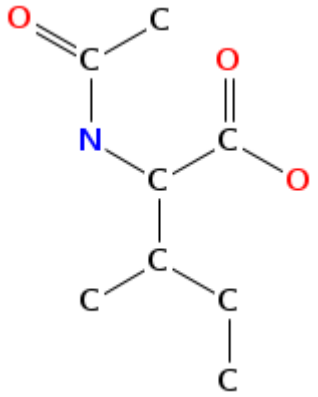




Are those monomers “PEPTIDE” ?



N-dimethyl-alanine



N-acetyl-Isoleucine

We consider yes as they are derivatives of an amino acid