Analyzing 3D-Structures:

CHEOPS Contact Analysis

**"Contacts as Favourable Interactions
offer a more *Chemists* View of Structures
than Cartesian or Crystallographic Coordinates"**

Introducing Contacts

- **Functionalities**
  Chemical functionalities prefer to act in certain directions (e.g. hydrogen bond donor/acceptor, π-systems etc.)
- **Contacts**
  Good interactions defined by spatially matching directions of complementary functionalities are called contacts, like

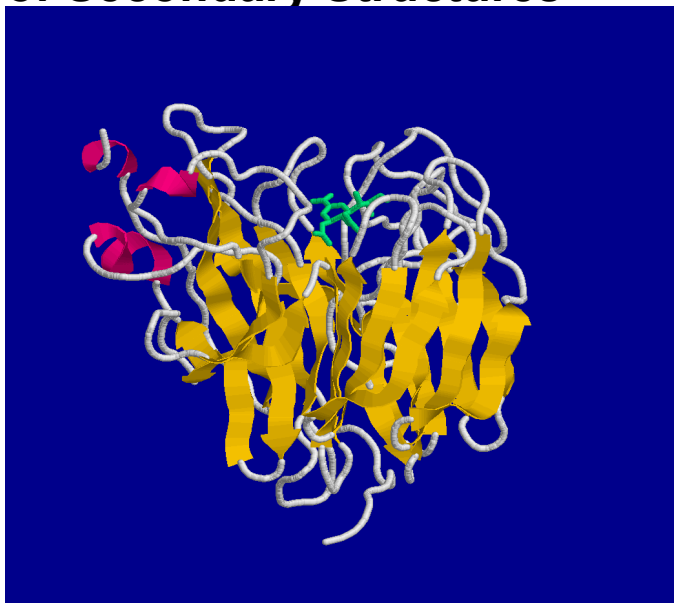
```
ASP330A        ARG364A      SASD                X
(residue-name residue-name type_of_contact presence)
```

- **Contact Vector**
  The full set of all contacts in a geometry is called the contact vector representing this geometry.
- **Groups of Contacts**
  Groups of centers (e.g. backbone, hetero-groups, water) build groups of contacts in the contact vector

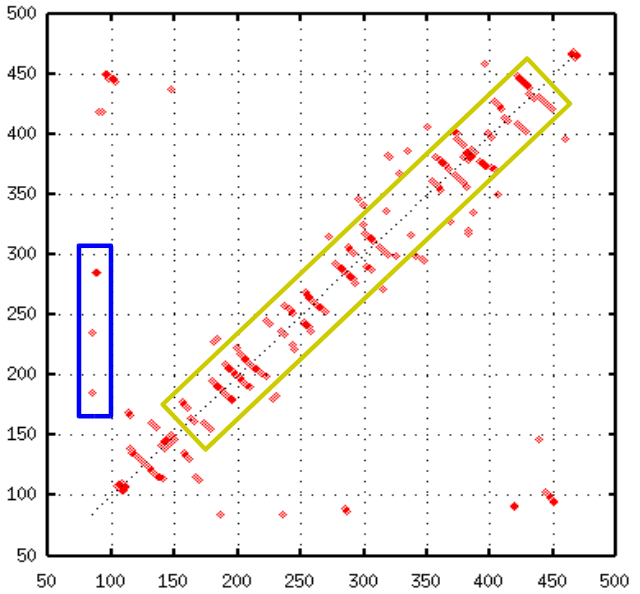
$\Rightarrow$ **coordinate-free representation of a geometry**

Representing Geometries

Standard Representation of Secondary Structures



Contact Diagram (backbone only)



(1NNC, 2.2Å, 1995)

The diagram visualizes secondary structure forming (e.g. antiparallel β-sheet) and other (e.g. long-range) contacts

⇒ **contact analysis gives insight into details of the structure**

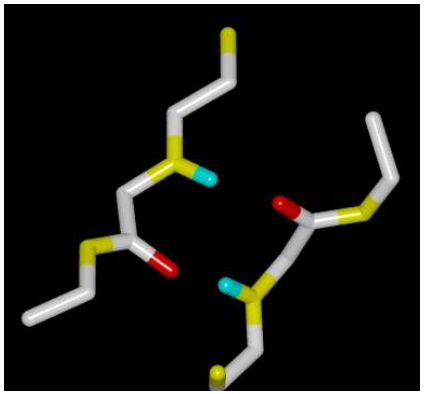
Specific Hydrogen Bond Contacts

Introducing *CHEOPS* Contacts and Notation

- **B**ackbone to **B**ackbone

TYR374A	VAL398A	BABD	X
TYR374A	VAL398A	BDBA	X

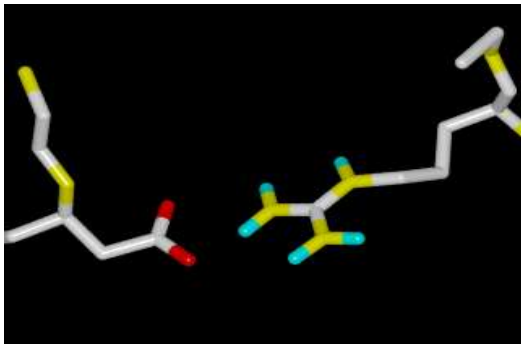
bi-directional backbone contact of two residues in an anti-parallel β-sheet



- **S**idechain to **S**idechain

ASP330A	ARG364A	SASD	X

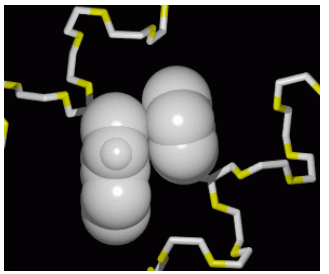
Donor/Acceptor interaction of ionizable sidechains in salt bridge

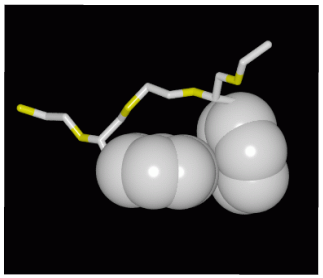


⇒ explore directed highly polar interactions ...

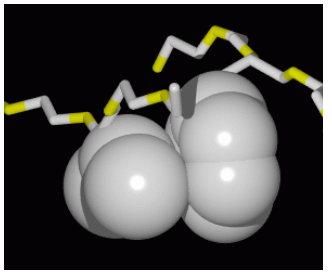
Van der Waals-Type Contacts of Sidechains

- Aromatic Ring-to-Ring Centered Contact
  e.g.: TRP393A PHE445A SSC X

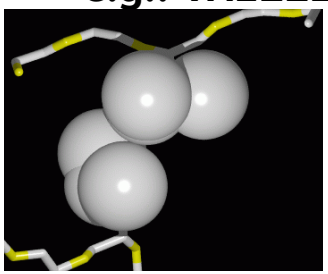




- Aromatic Rings Edge-to-Ring Contact
  e.g.: PHE383A PHE385A SESR X



- Alkyl-to-Aromatic Ring vdWaals Contact
  e.g.: VAL122A PHE410A SASR X



- Alkyl/Alkyl unspecific vdWaals Contact
  e.g.: LEU268A ILE275A SSV X

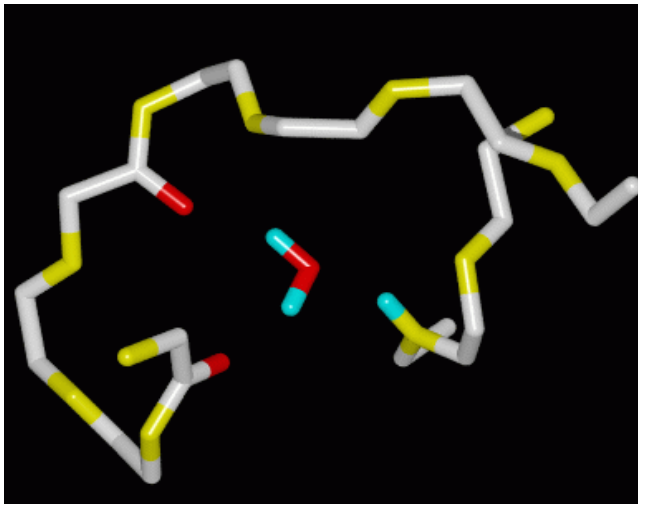
⇒ explore aromatic ring and alkyl group nonpolar interactions ...

Multiple Contacts: Essential Water

Essential Water Molecules are Part of a Protein

Water molecules in a hydrogen bond network bridging protein functionalities show up with multiple contacts like:

HOH6B	GLY109A	SDBA	X
HOH6B	SER112A	SDBA	X
HOH6B	ARG141A	SABD	X



⇒ **get insight into important structural features ...**

Inhibitor Binding at a Glance

Binding of Inhibitor given by its Group Contacts

Example: Inhibitor Binding in Neuraminidase (PDB:1NNC)

HBO contacts to backbone

HET3/L3A	GNA200B	ASP151A	SDBA	X
HET3/x9A	GNA200B	TRP178A	SDBA	X

HBO contacts to sidechain

HET3/B1EA	GNA200B	ARG118A	SASD	X
HET3/L3A	GNA200B	ASP151A	SDSA	X
HET3/L3A	GNA200B	ARG152A	SASD	X
HET3/L14A	GNA200B	ARG371A	SASD	X

VDW contacts to sidechain

HET3/x9A	GNA200B	TRP178A	SSV	X
HET3/L7A	GNA200B	ILE222A	SSV	X
HET3/B1GA	GNA200B	ARG224A	SSV	X
HET3/L9A	GNA200B	ALA246A	SSV	X
HET3/B2HA	GNA200B	ARG292A	SASR	X
HET3/x21A	GNA200B	TYR406A	SSV	X

HBO contact to water

WAT/HET3	HOH123B	GNA200B	SDSA	X
WAT/HET3	HOH285B	GNA200B	SDSA	X

Bridging water

WAT/L8A	HOH121B	GLU227A	SDSA	X
WAT/x14A	HOH121B	GLU277A	SDSA	X
WAT/HET3	HOH121B	GNA200B	SASD	X

⇒ **groups of inhibitor contacts yield intuitive binding picture**

Contact Representation of Geometries

- Definition of Contacts Yields Favourable Interactions
- Complete Set of Specific and Unspecific Interactions
  - type of functionality (e.g.: donor, acceptor, alkyl)
  - type of interaction (e.g.: HBO, VDW)
  - type of residue (e.g.: amino acid, hetero-group, water)
  - location in residue (e.g.: backbone, sidechain)
  - secondary structure element of residue
- Data Reduction (1000:1)
- Easy to Handle ASCII-Data

Contact Vector Gives a
More Intuitive Picture
of the Structure

⇒ *CHEOPS* contact analysis can also represent dynamics ...