

Molovol An Easy-to-Use Tool for Calculating Cavity Volumes and Surfaces

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Receptors in host-guest chemistry are (supra)molecular structures that often present a cavity able to nest guests. Characterizing the shape and properties of these cavities can be useful to evaluate potential matching guests and to understand the interactions in a host-guest complex. MoloVol is a program that can calculate the volumes and surface areas of molecules and their cavities. MoloVol is free and operates via a user-friendly interface on Windows, macOS and Linux.

Website: https://molovol.com/

J. B. Maglic, R. Lavendomme, *ChemRxiv* **2021**, preprint, DOI: <u>10.33774/chemrxiv-2021-dss1j</u>



Closed cavity A spherical probe can define the space that is accessible by guests in a cavity

Open cavity No physical limit Need to define arbitrary limits Problem: Small probes cannot define

the limits of open cavities

Solution 1: Use large probes that cannot exit **Problem:** Narrower parts of the cavity are not defined properly (volume is underestimated)

Solution 2:

Use two probes, one large to define the outside space and one small to define the cavity

Case study 1: open cage with wide gaps

Pd₆L₄(bipy)₆ octahedral cage Yoshizawa et al., J. Am. Chem. Soc. 2005, 127, 2798-2799





Single-probe mode Probe radius: 3.3 Å Cavity volume: 443 Å³ (smaller probes can exit) **Cavity shape difference** between single- and two-probe modes **51% volume increase!**

Two-probe mode

Small probe radius: 1.2 Å Large probe radius: 5.0 Å Cavity volume: 669 Å³

Case study 2: deep cavitand and open macrocycle

Resorcinarene-based deep cavitand Amrhein *et al., J. Am. Chem. Soc.* **2002**, *124*, 10349-10358 **Decaethyl pillar**[5]arene

Li et al., Angew. Chem. Int. Ed. 2020, 59, 22012-22016



In both cases, the openings are too large to define a cavity with a single probe

Two-probe mode Small probe radius: 1.2 Å Large probe radius: 3.0 Å Cavity volume: 295 Å³

Two-probe mode

Small probe radius: 1.2 Å Large probe radius: 3.0 Å Cavity volume: 189 Å³



Case study 3: giant open cage

Pd₄₈L₉₆ giant coordination cage Fujita *et al., Nature* **2016**, *540*, 563-566



Other possible outputs: various types of volumes and surface areas

Fe^{II}₄L₆ open cage Yamashina *et al., Nature* **2019**, *574*, 511-515





Single-probe mode Probe radius: 6.0 Å Cavity volume: 86 526 Å³

Using two probes is possible but unnecessary as asperities are negligible compared to the bulk volume (note: Calculation performed on a crystal structure not containing hydrogen atoms and after removal of counter-anions)