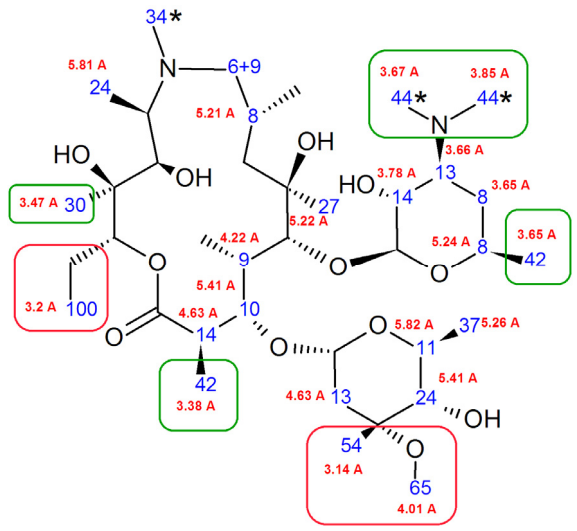
Interactions between Macromolecules and their Ligands in Solution State

Objectives

- to compare the free and bound structures of several macrolides possessing a variety of biological activities
- to identify areas of the macrolide which are the closest to the *E. coli* ribosome surface and are most likely involved in binding to the active site

- Analysis of trNOESY experiments showed that macrolide conformation does not change significantly upon binding to the *E. coli* ribosome
- STD NMR can be used to monitor the interactions between macrolides and ribosome
  - competition experiment has proved the examined macrolide binds to the active site
  - STD enhancements observed for azithromycin and distances between azithromycin and ribosome (determined in X-ray co-crystallized structure of azithromycin and *H. marismortui)* showed a good correlation.



Comparison of STD signal enhancements and distances from ribosome taken from X-ray structure of co-crystallized azithromycin with *H. Marismortui* (*peak overlap)

- Macrolides have three distinct areas which are the closest to the ribosome:
  - methyl group 15 (macrocyclic ring)
  - 3"Me and 3"OMe (cladinose)
  - dimethylamino group (desosamine)

References:
P. Novak et al., J.*Bioorgan. Med. Chem.* **17** (2009) 5857-5867.

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