

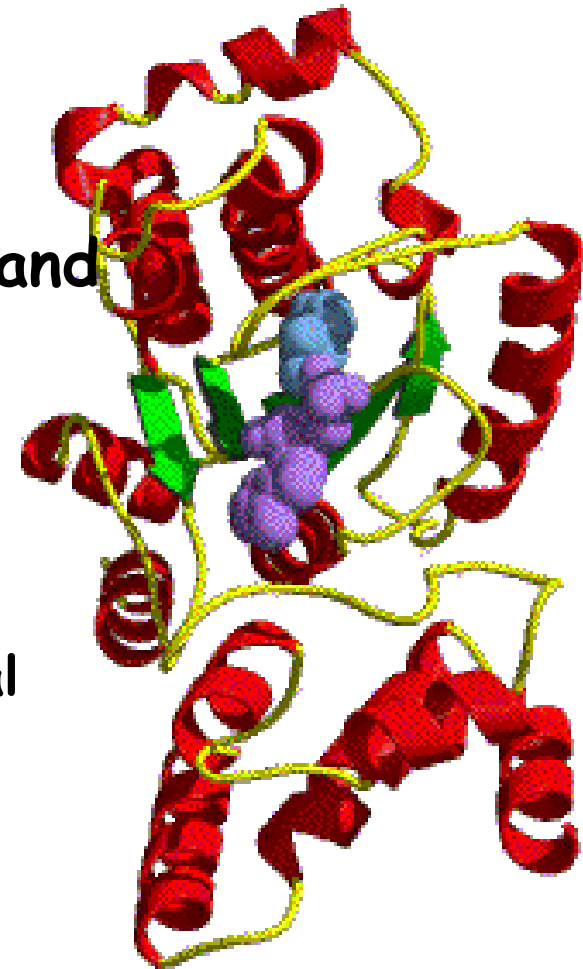
Structure of C -terminal Domain of Tyrosyl-tRNA Synthetase from *Mycobacterium tuberculosis*

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Advisor: Dr. Hans D. Bartunik

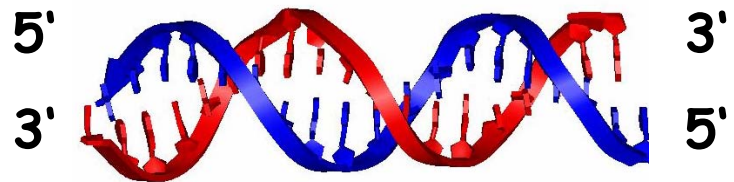
Trainer: Dr. Gleb Bourenkow

Max-Planck Unit for Structural
Molecular Biology, HASYLab



Introduction

DNA

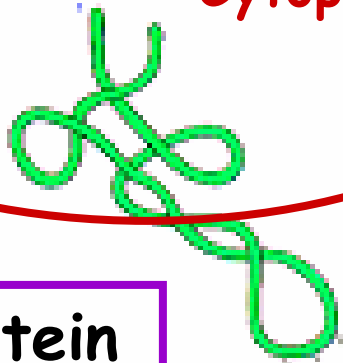


Transcription
Nucleus

5' 3'

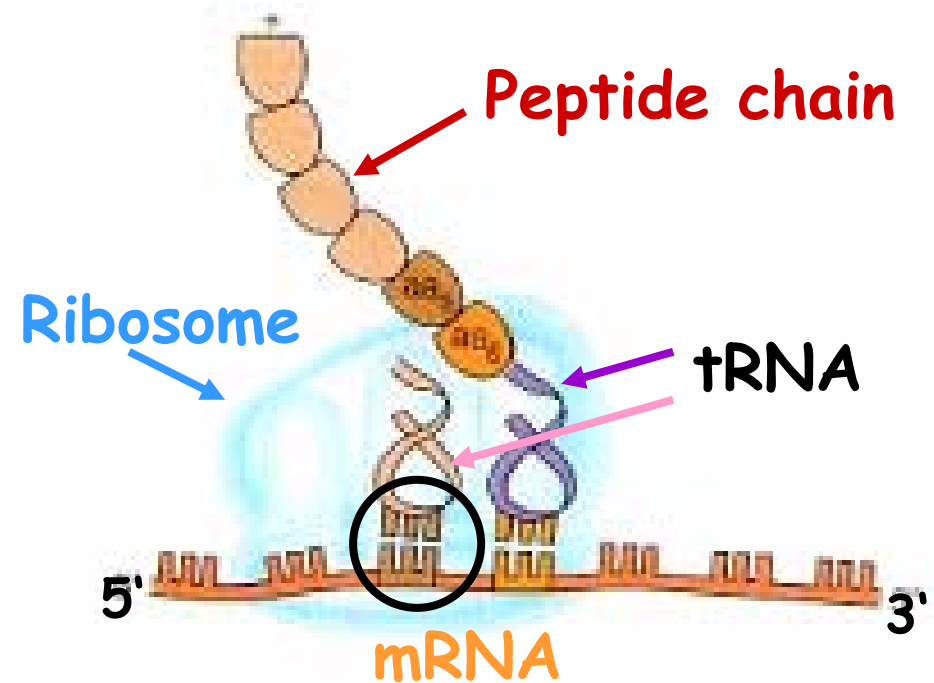
mRNA

Translation
Cytoplasm



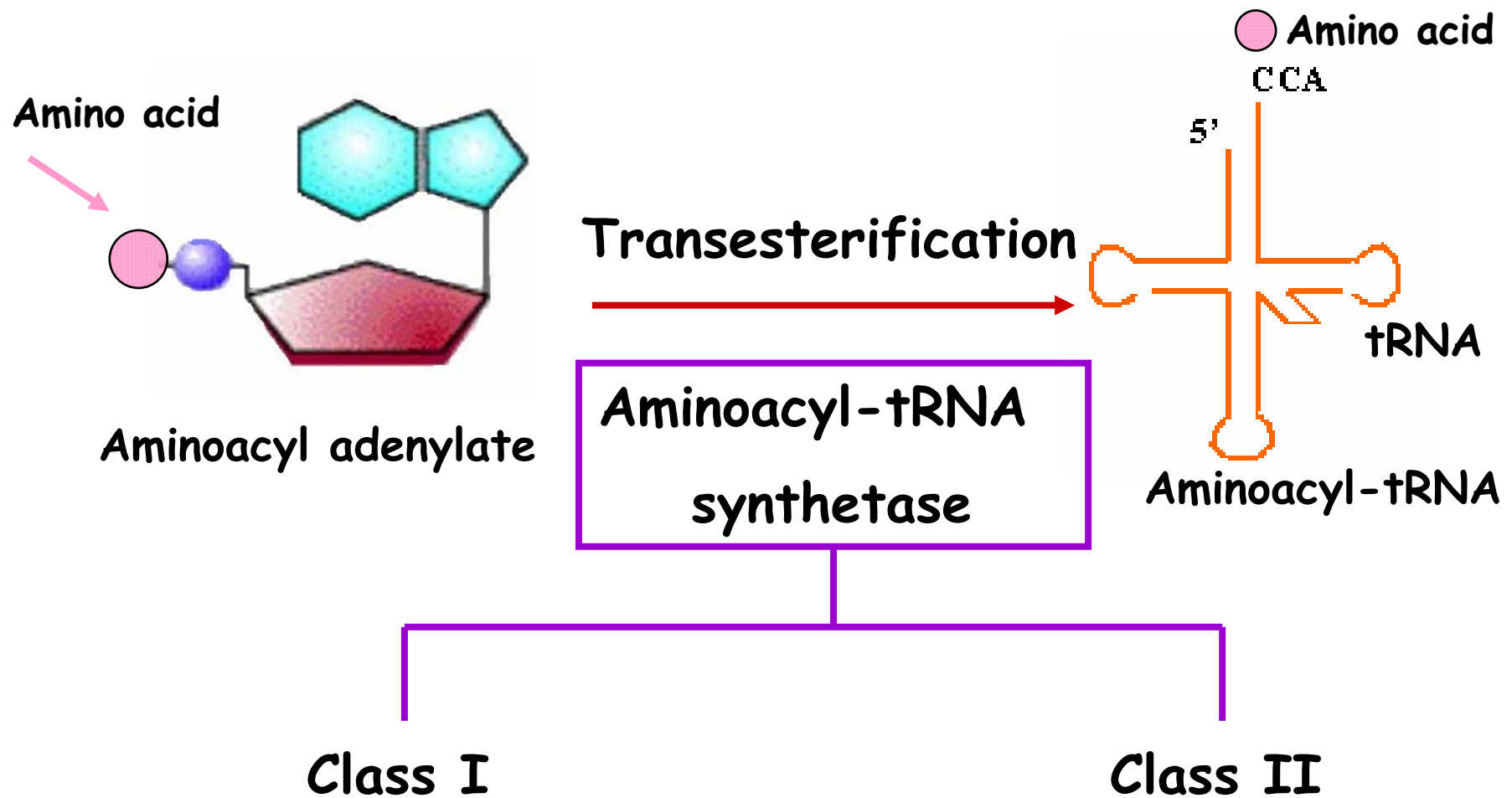
Protein

Protein Biosynthesis

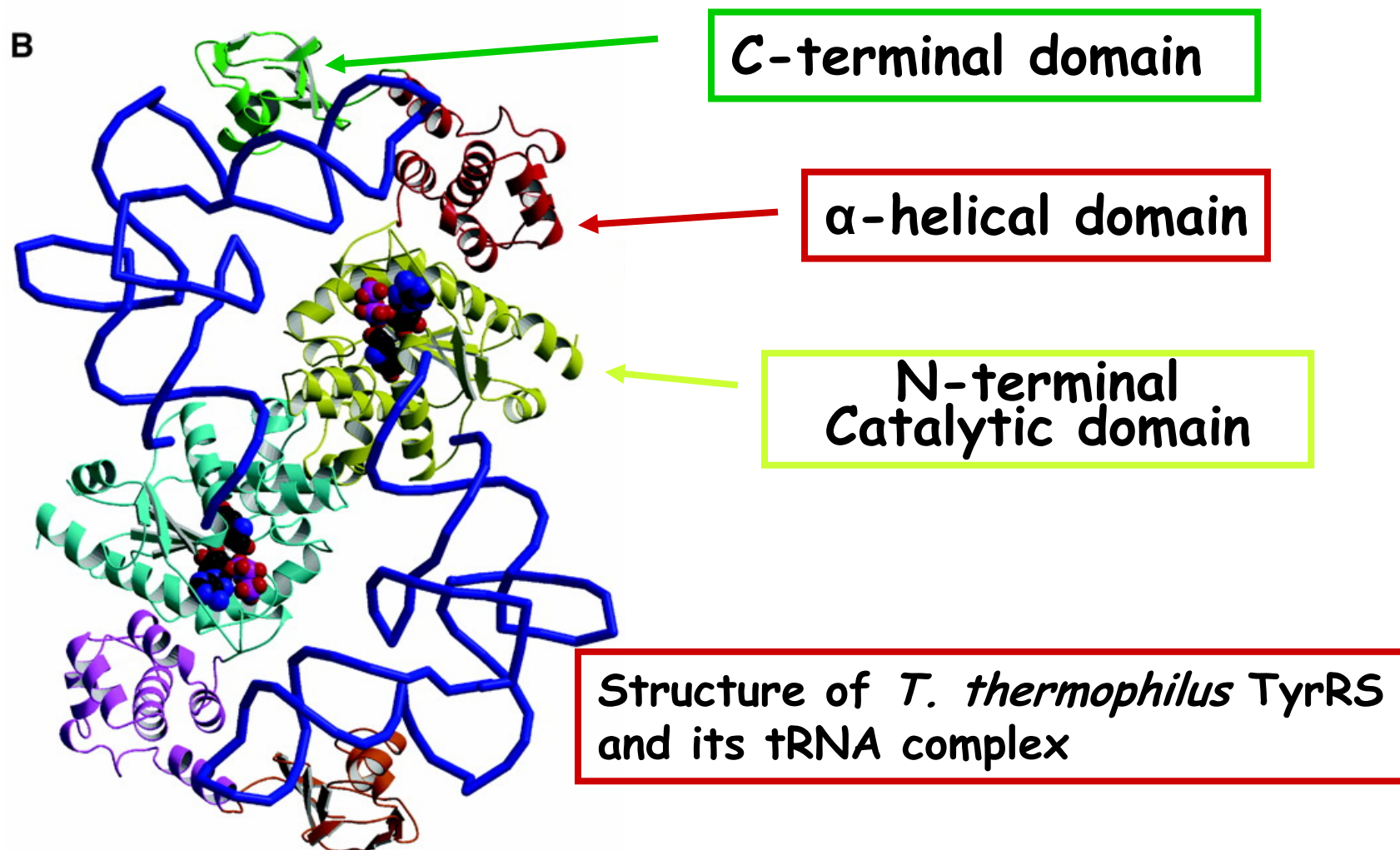


Modified from Griffiths et al., An Introduction to Genetic Analysis, 6th Ed., W.H. Freeman & Co., 1996

How tRNAs attach their amino acids?



Tyrosyl-tRNA Synthetase (TyrRS)



Yaremchuk, A., et al (2002) *EMBO J.* 21, 3829-3840.

Objective

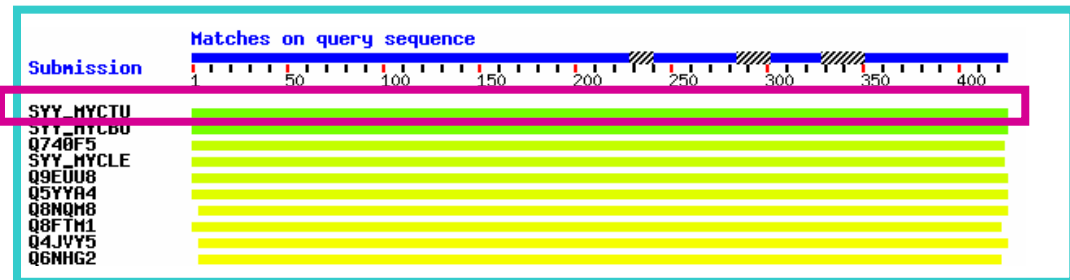
- ❏ Crystal structure determination of C-terminal domain of TyrRS from *Mycobacterium tuberculosis* for drug design

Methods

M. Tuberculosis TyrRS
424 amino acids

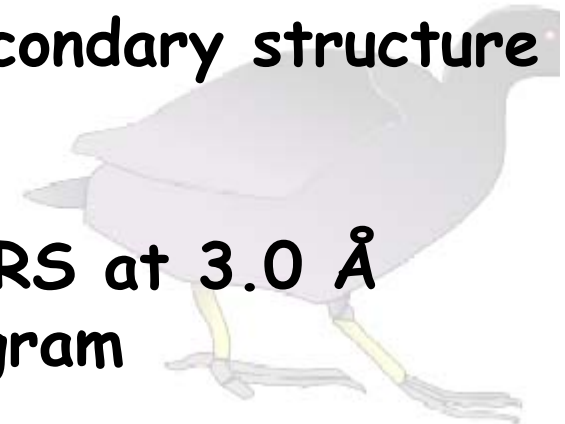
10	20	30	40
MSGMILDELS	WRGLIAQSTD	LDTLAAEAQR	GPMTVYAGFD
50	60	70	80
PTAPSLHAGH	LVPLLTLLRF	QRAGHRPIVL	AGGATGMIGD

Search similarity

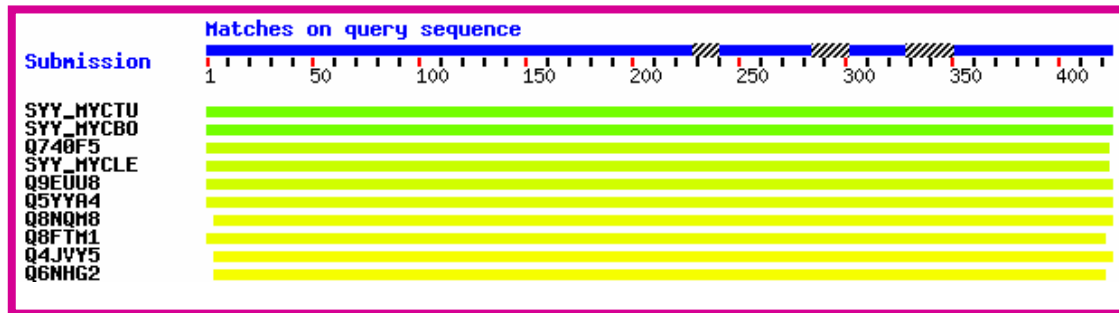


Run multiple alignment and alignment of secondary structure

X-ray data of *M. Tuberculosis* TyrRS at 3.0 Å
resolution (BW6), Coot Program



Results and Discussion



B. stearothermophilus,
S. aureus,
E. coli TyrRSs

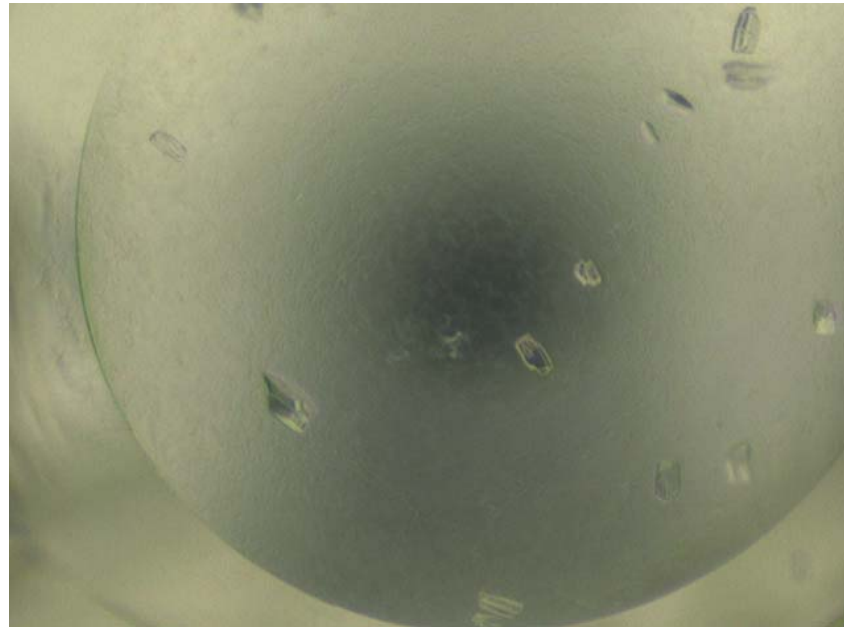


	SSSTTS HHHHHHHHTTS EEEE SS HHHHHHHHTS
<i>B. stearothermophilus</i>	ALFS-GDIANLTAAEIEQGFKDVPSFVHE-GGDVPLVELLVSAGISP
	::: :...: : : . : : : : : : : : : : :
<i>M. tuberculosis</i>	ALFGRGELARLDEATLAAALRETTVAELKPGSPDGIVDLLVASGLSA



B. stearothermophilus TyrRS



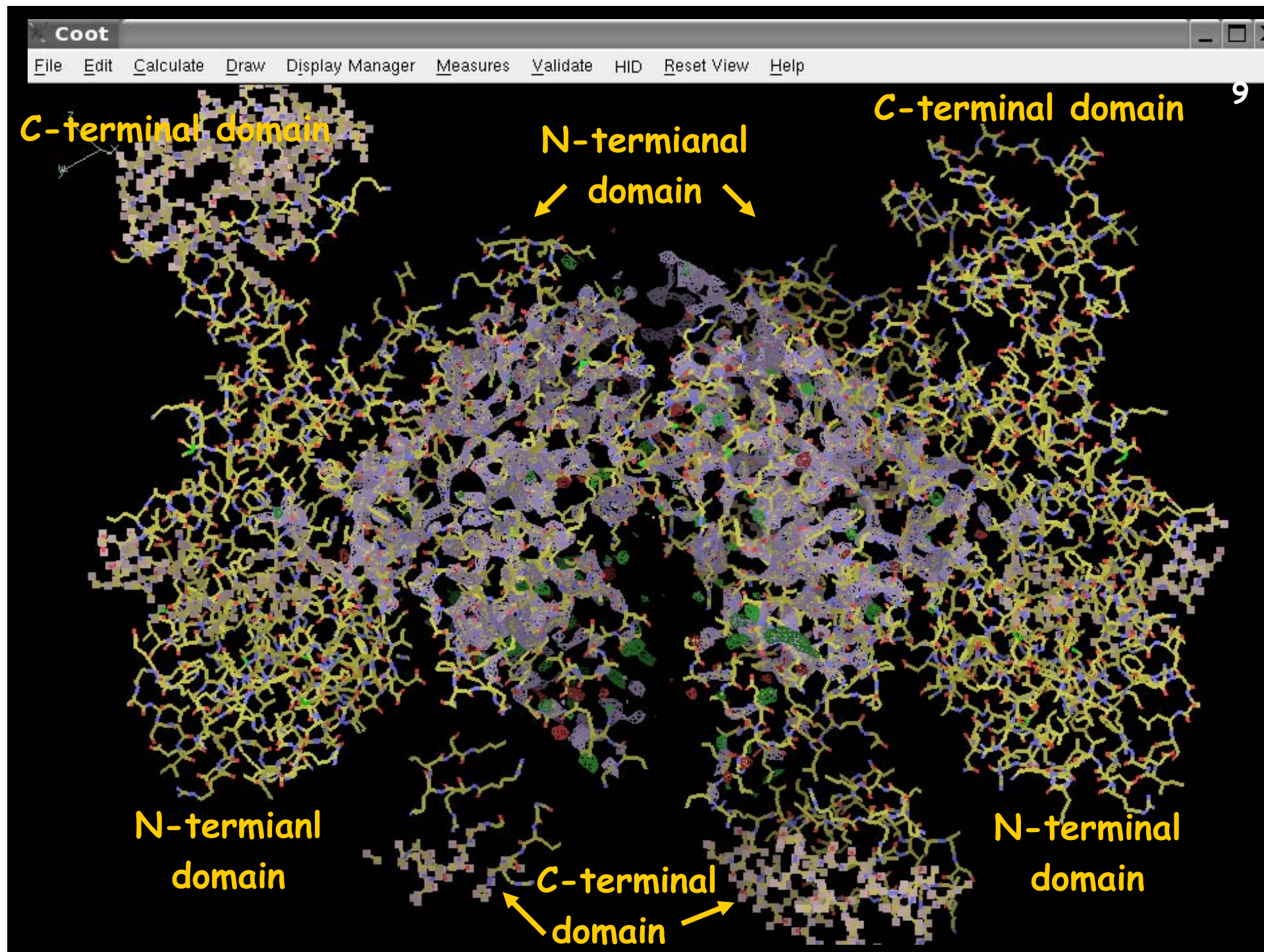


X-ray data of *M. Tuberculosis* TyrRS
at 3.0 Å resolution (BW6)



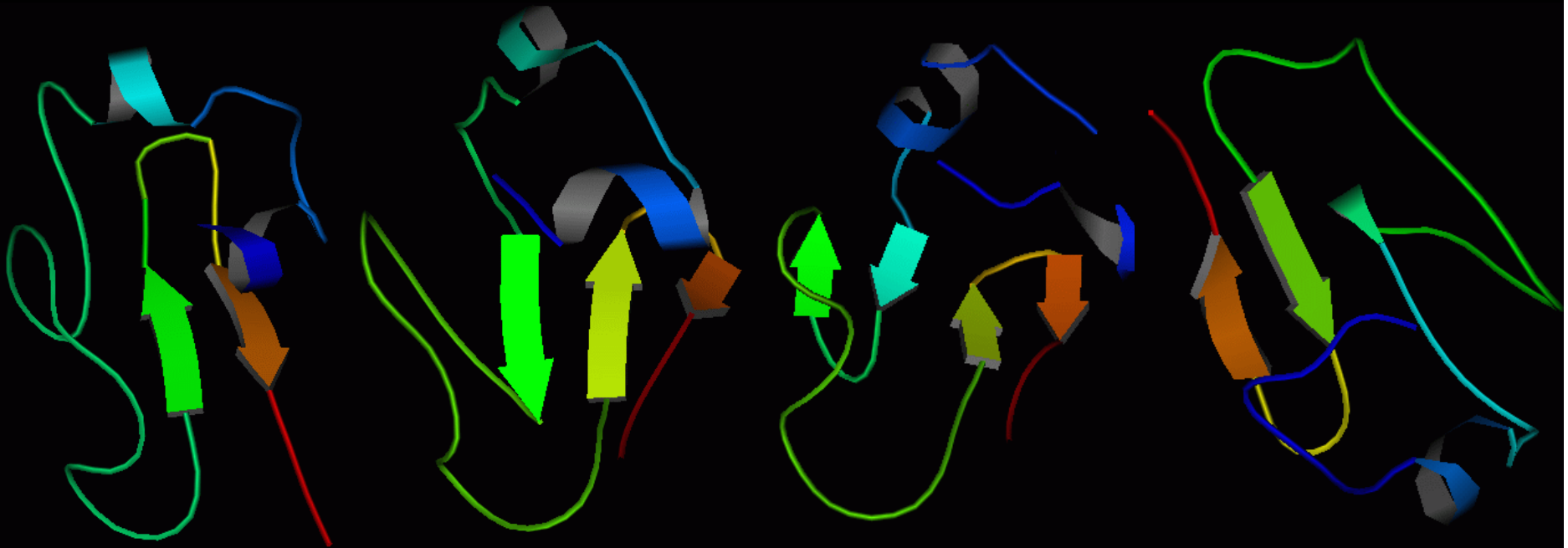
**Molecular Replacement
Calculation of Phases**

4 TyrRS molecules in asymmetric unit
N-terminal and C-terminal domain structures



Structures of 4 C-terminal domains

Molscript



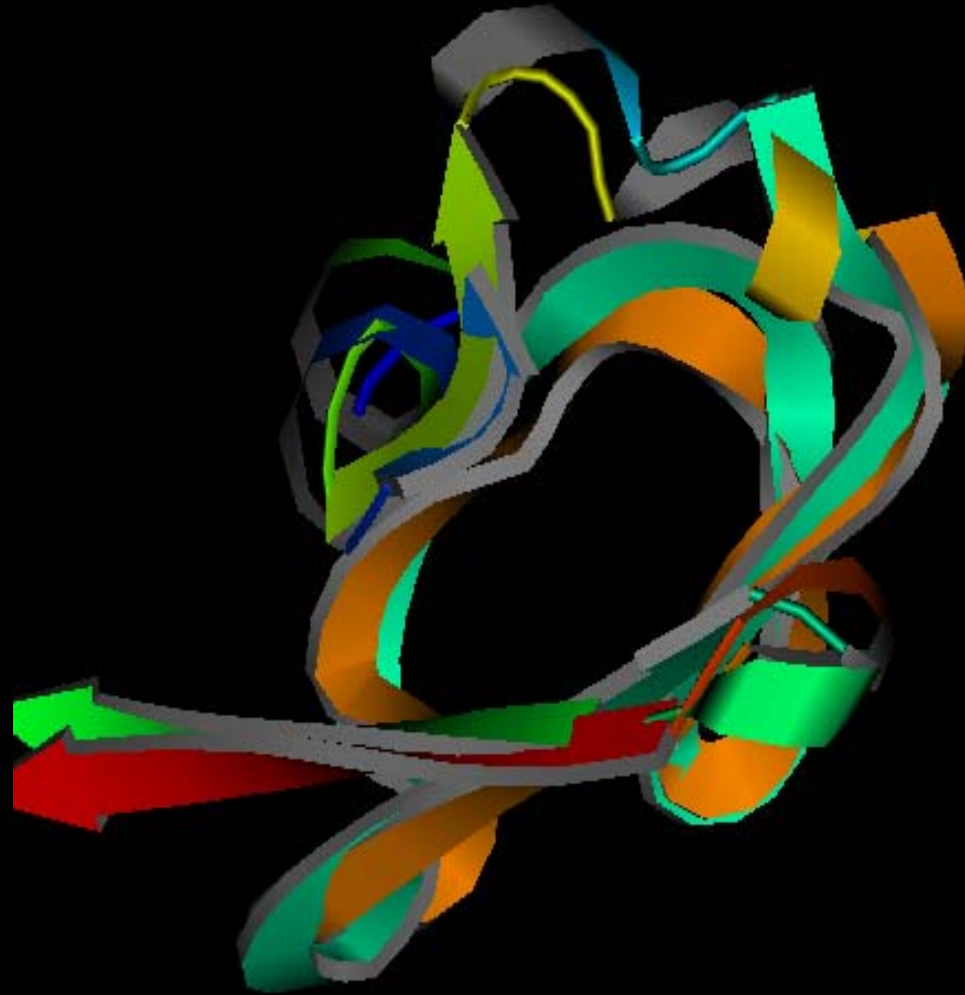
Domain 1

Domain 2

Domain 3

Domain 4

Superposed model of 4 C-terminal domains



360
VD

370 380 390 400 410 420
LLVASGLSAS KGAARRTIHE GGVSVNNIRV DNEEWVPQSS DFLHGRWLVL RRGKRSIAGV

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- All members of the Bartunik group