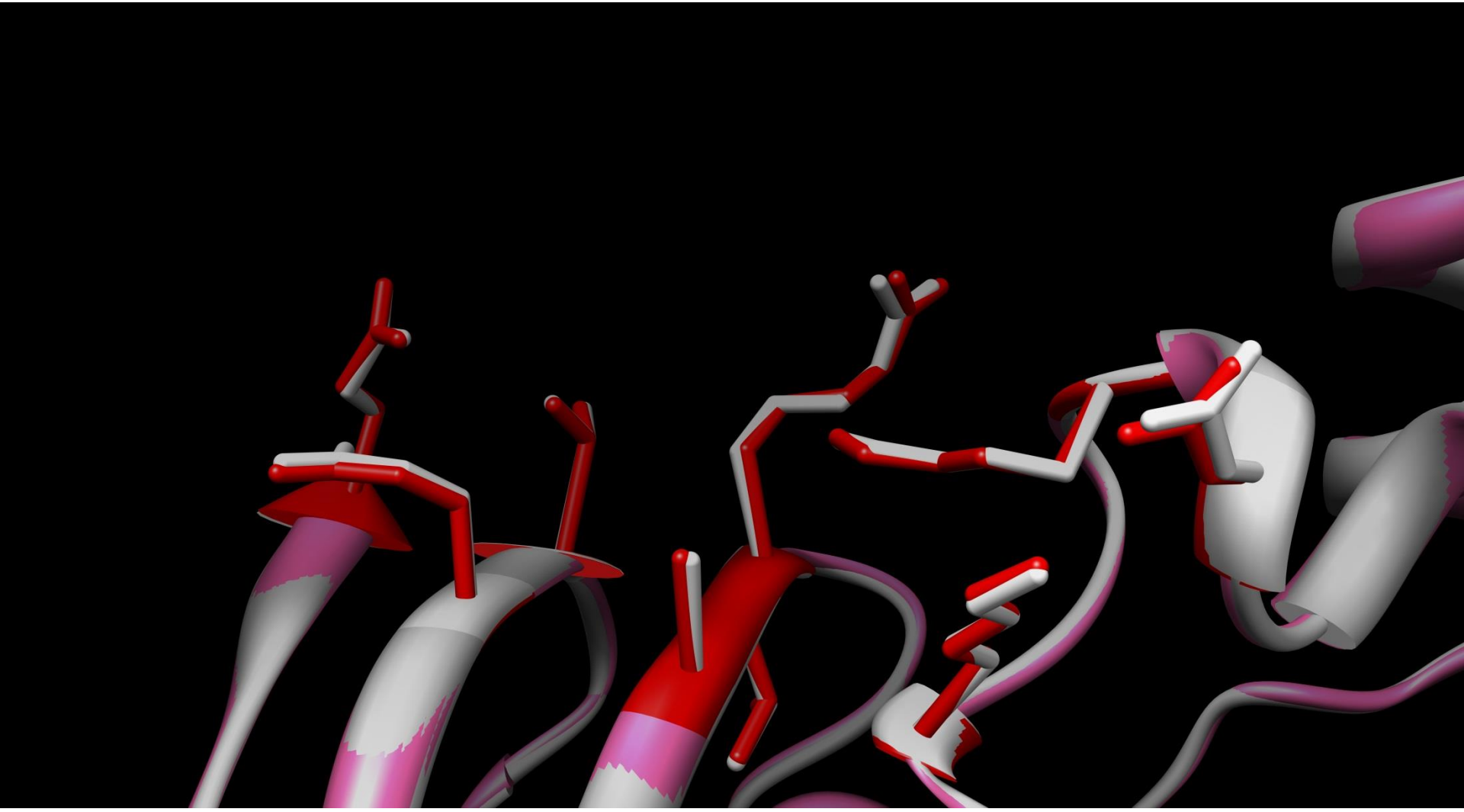
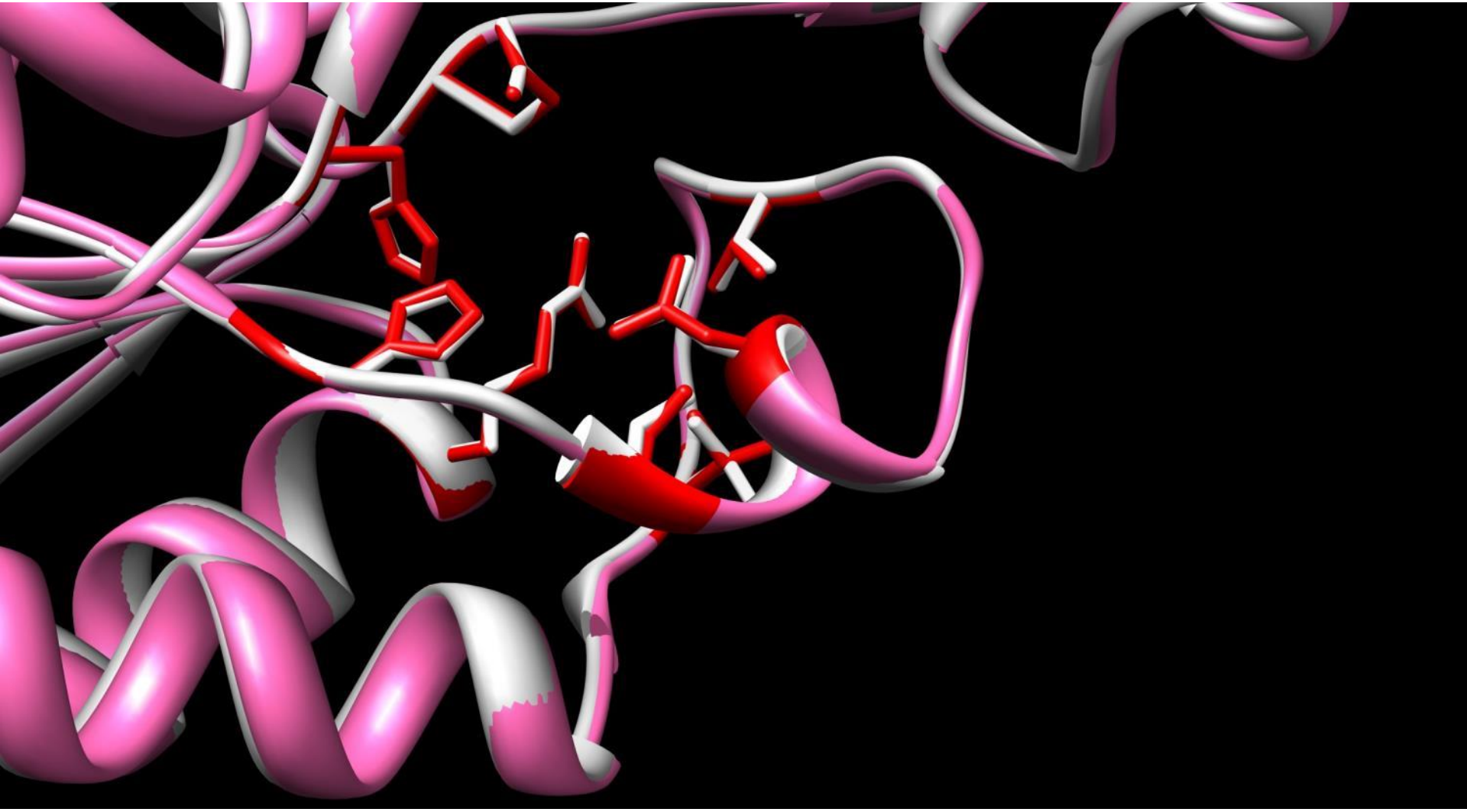
Dataset S1. Enzyme active site superpositions. Active site superpositions for all mycobacterial enzyme pairs in the same OrthoMCL family, in order of decreasing active site similarity (PS_{APF}).

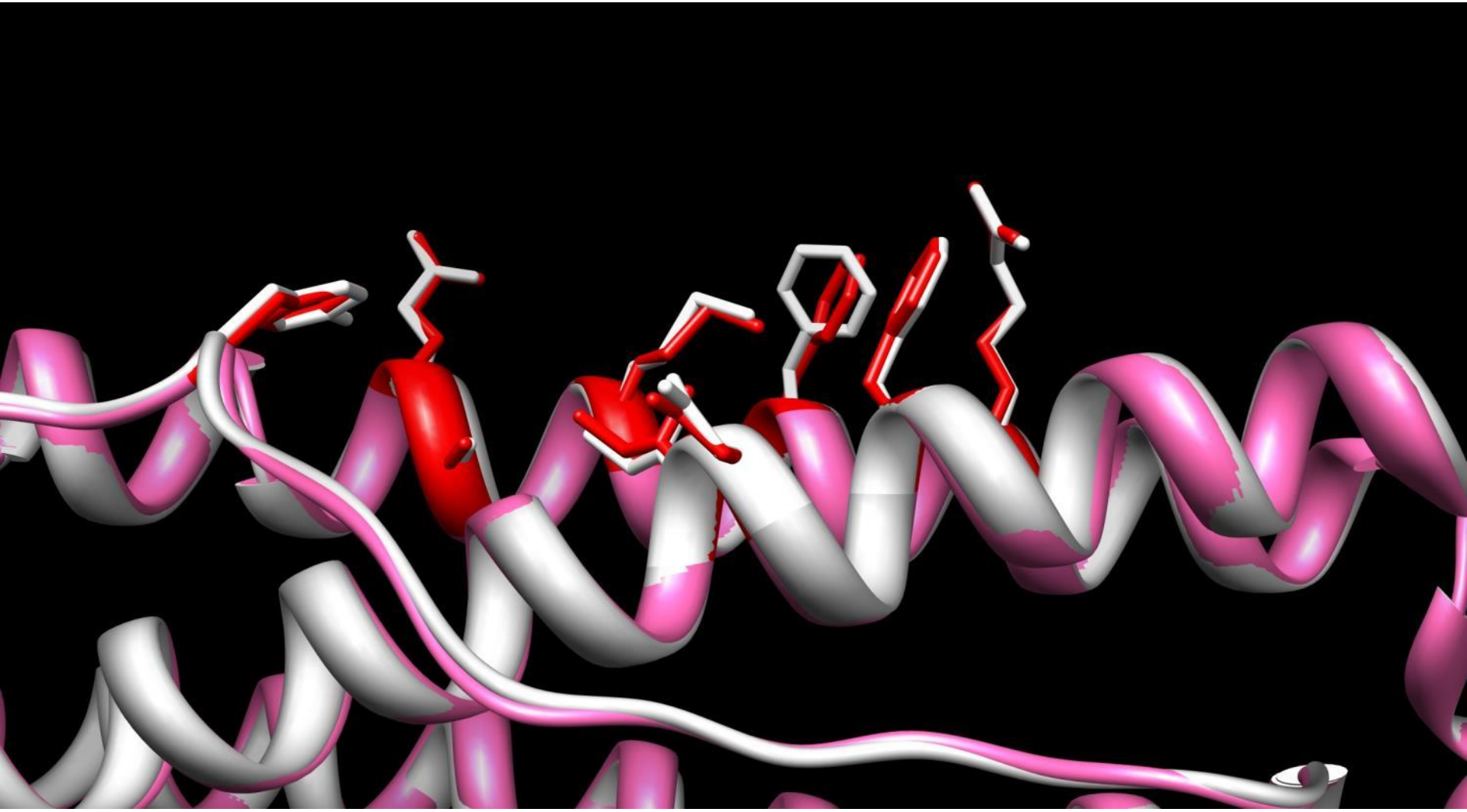
1. Mtb metK (PDB:3TDE, white), *M. marinum* metK (3RV2, red/pink)
Sequence identity 95%, PS_{APF} 99%



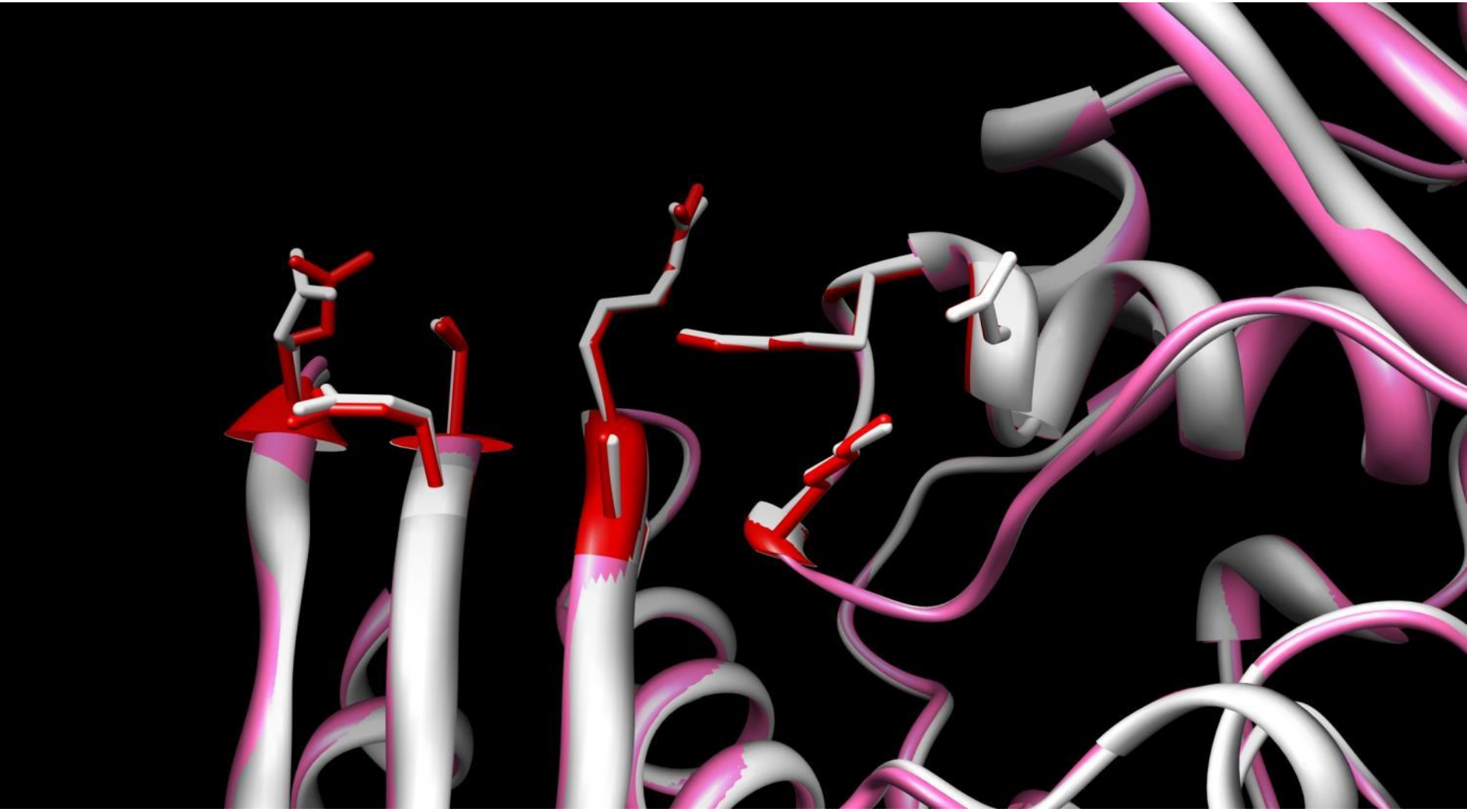
2. Mtb gpmA (PDB:1RII, white), *M. leprae* gpmA (4EO9, red/pink)
Sequence identity 89%, PS_{APF} 99%



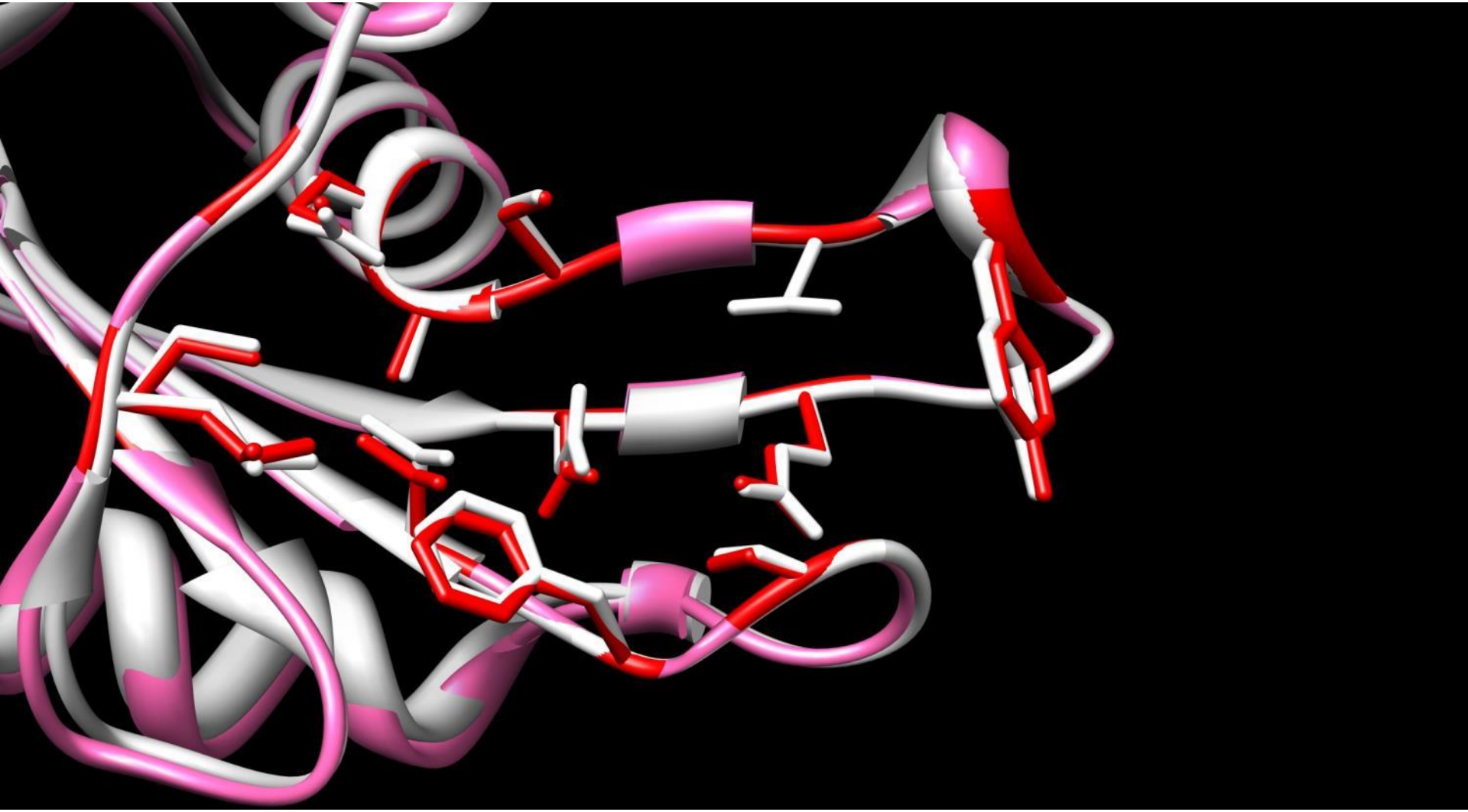
3. Mtb bfr (PDB:2WTL, white), *M. smegmatis* bfr (3BKN, red/pink)
Sequence identity 88%, PS_{APF} 97%



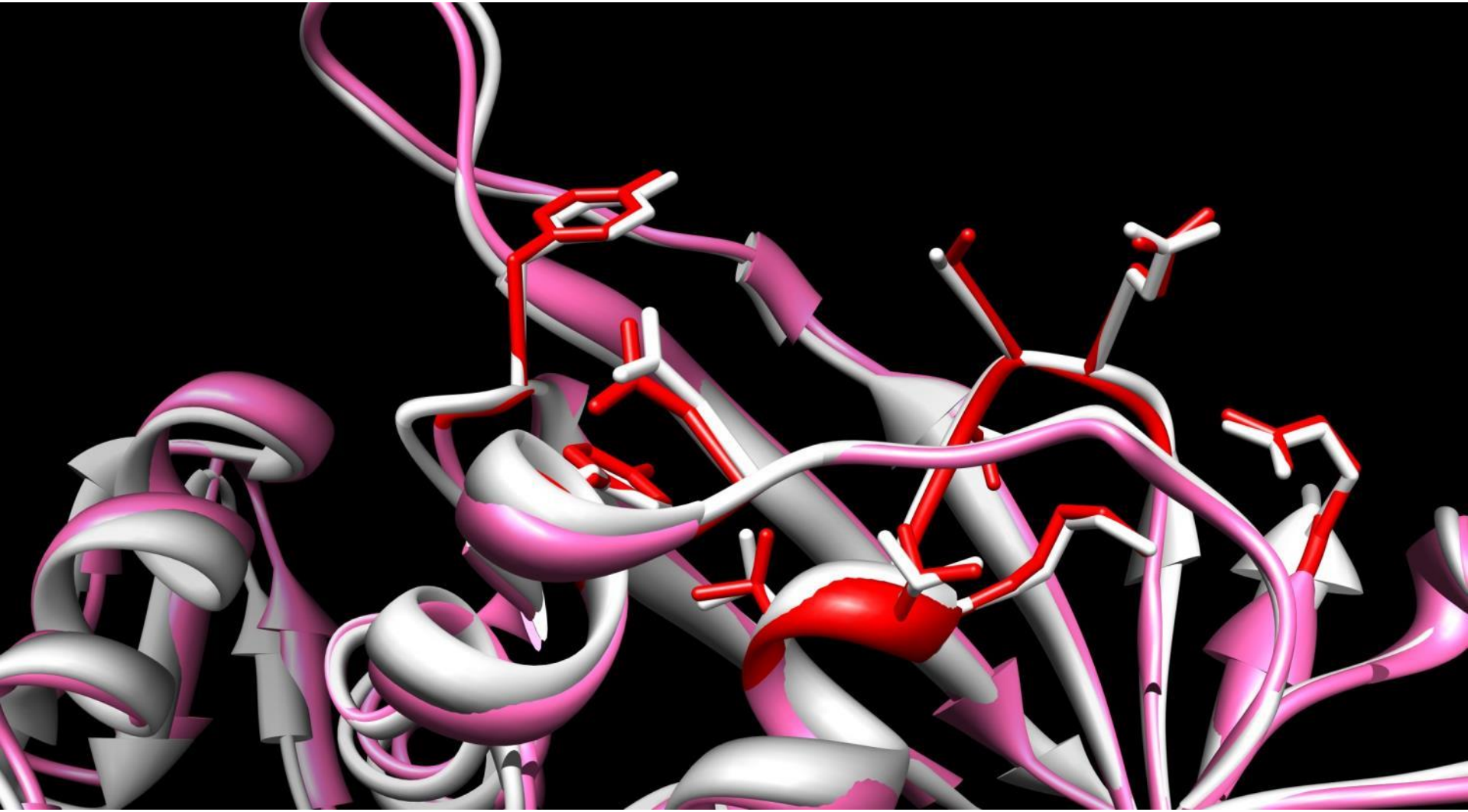
4. Mtb metK (PDB:3TDE, white), *M. avium* metK (3S82, red/pink)
Sequence identity 92%, PS_{APF} 96%



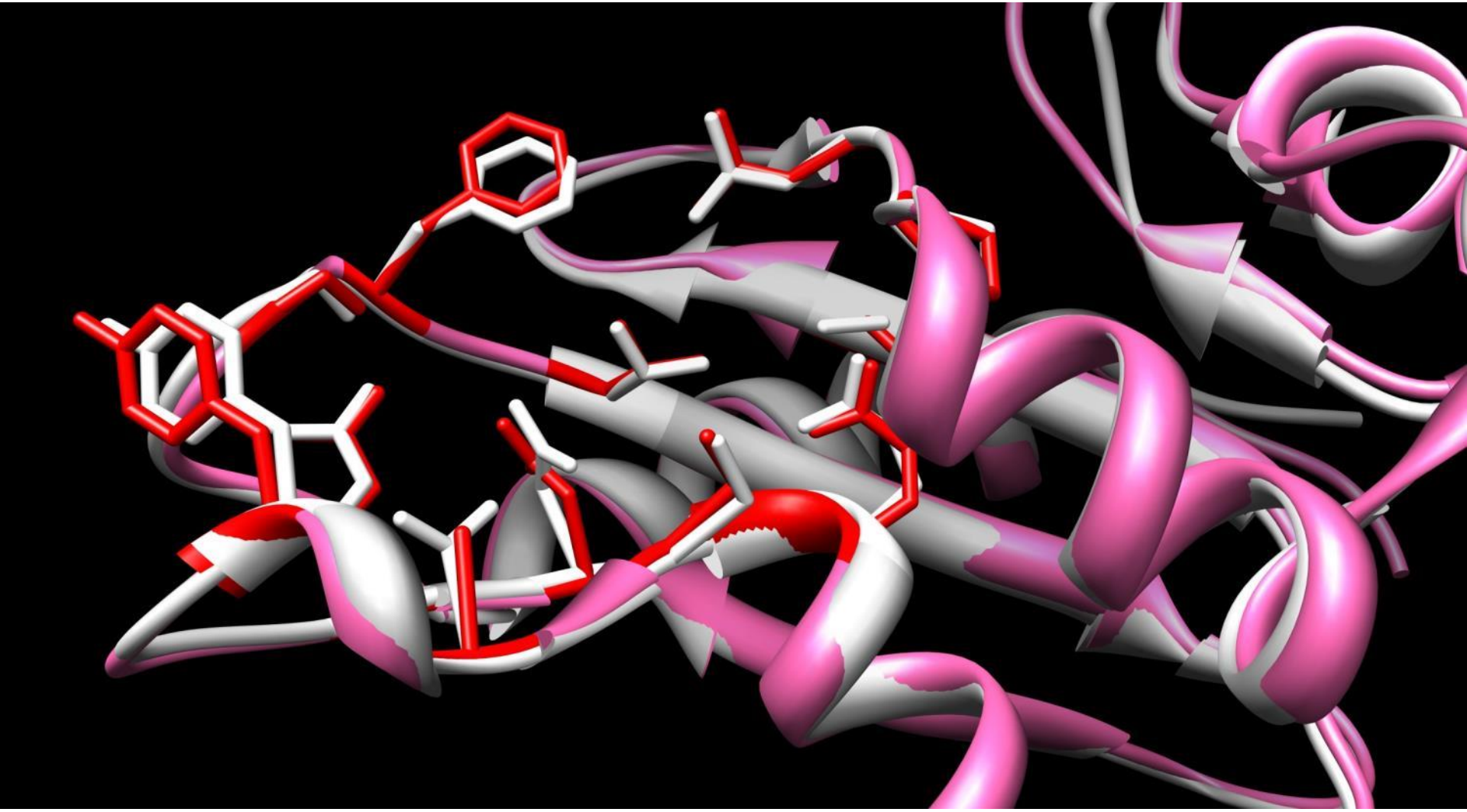
5. Mtb cdd (PDB:3IJF, white), *M. smegmatis* cdd (3MPZ, red/pink)
Sequence identity 75%, PS_{APF} 94%



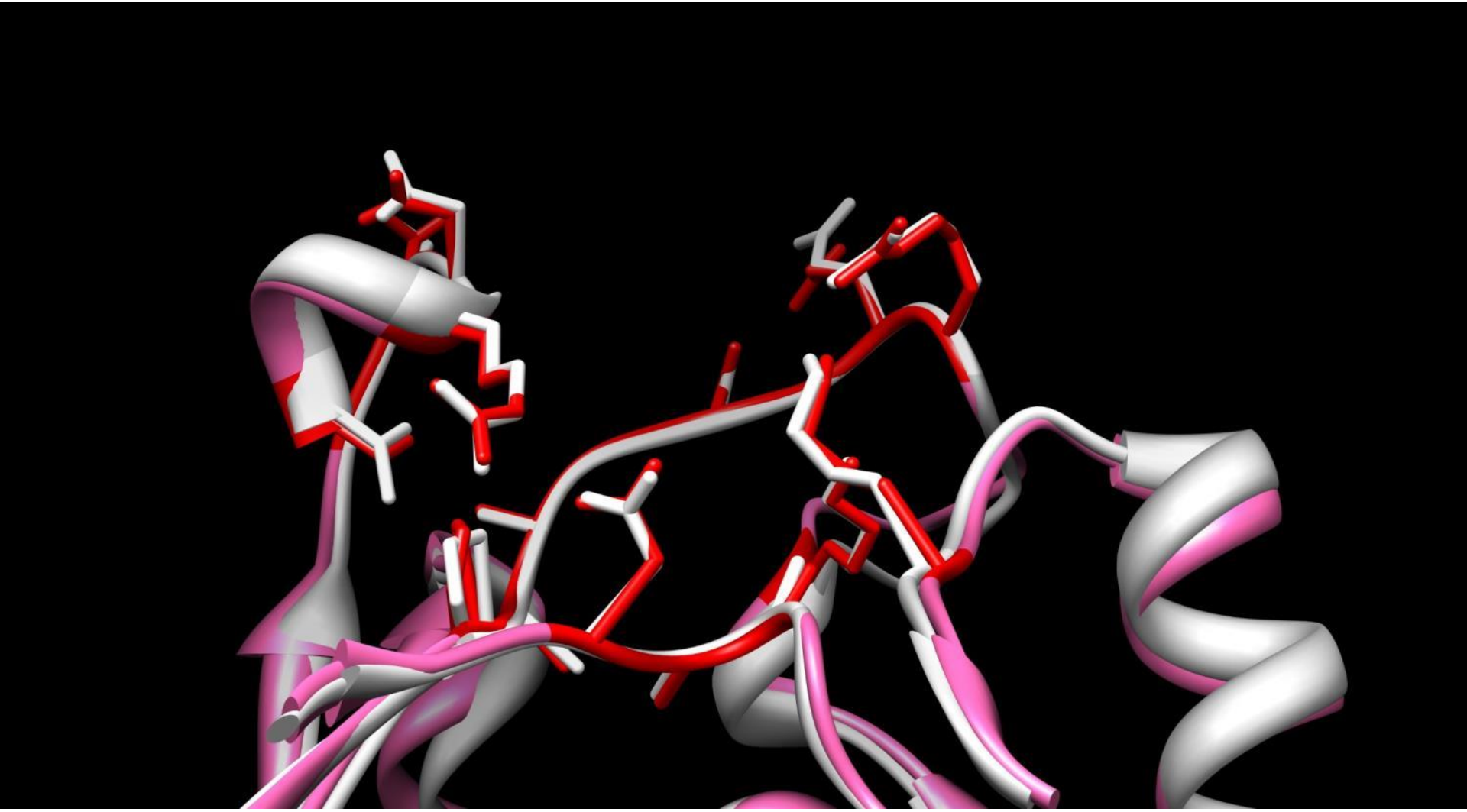
6. Mtb recA (PDB:1G19, white), *M. smegmatis* recA (1UBC, red/pink)
Sequence identity 93%, PS_{APF} 94%



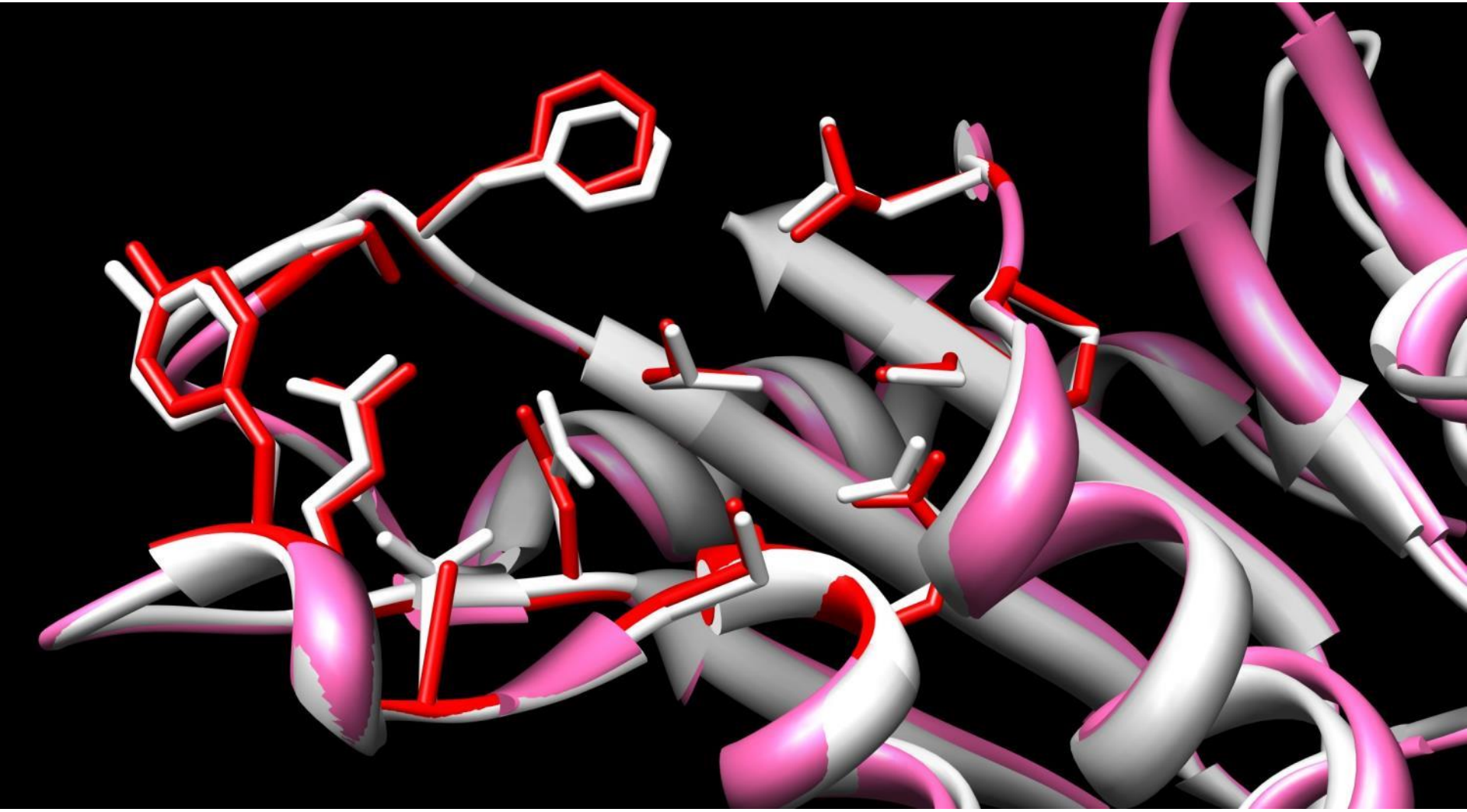
7. Mtb cdd (PDB:3IJF, white), *M. marinum* cdd (4F3W, red/pink)
Sequence identity 79%, PS_{APF} 93%



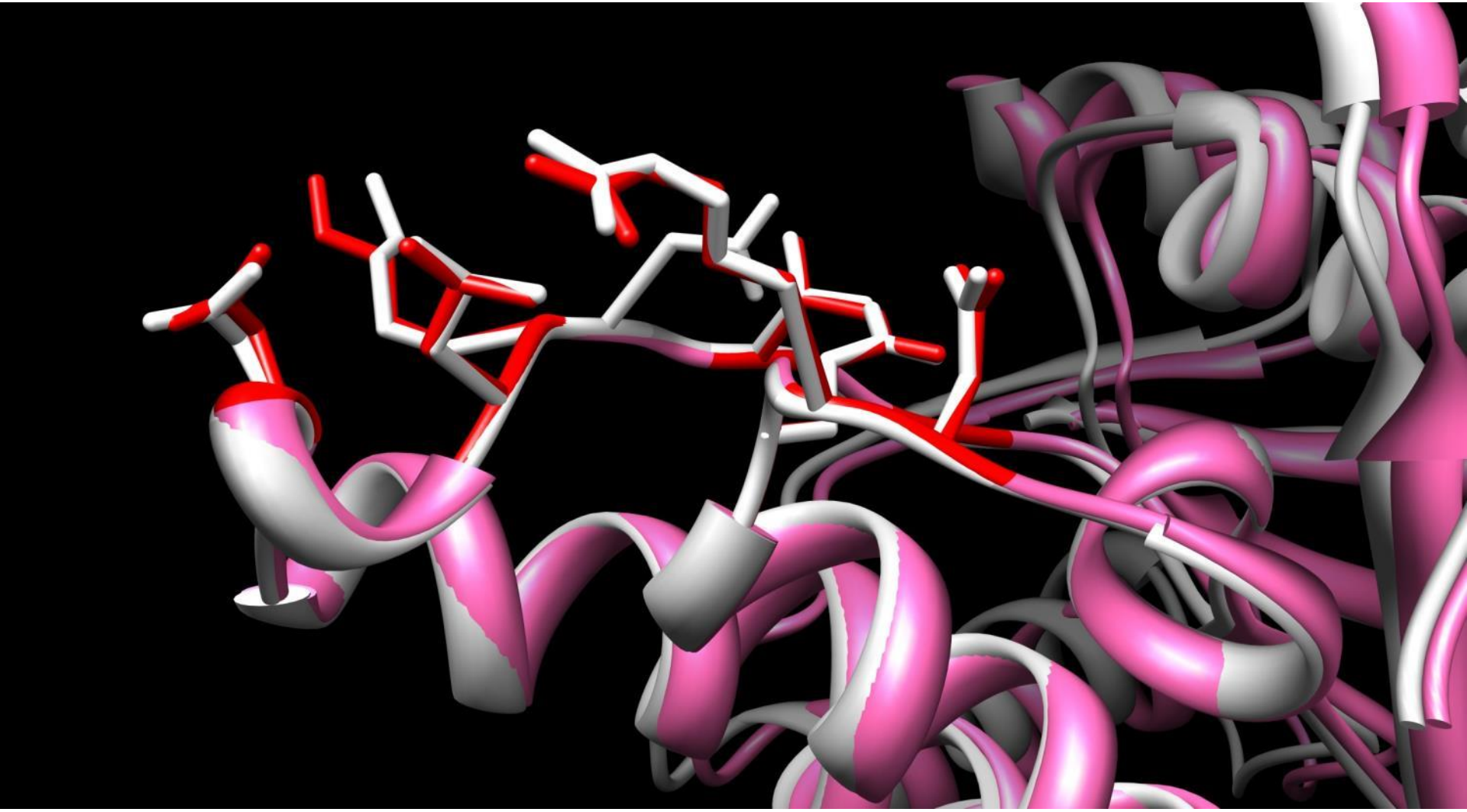
8. Mtb ispD (PDB:2XWN, white), *M. smegmatis* ispD (2XWL, red/pink)
Sequence identity 63%, PS_{APF} 93%



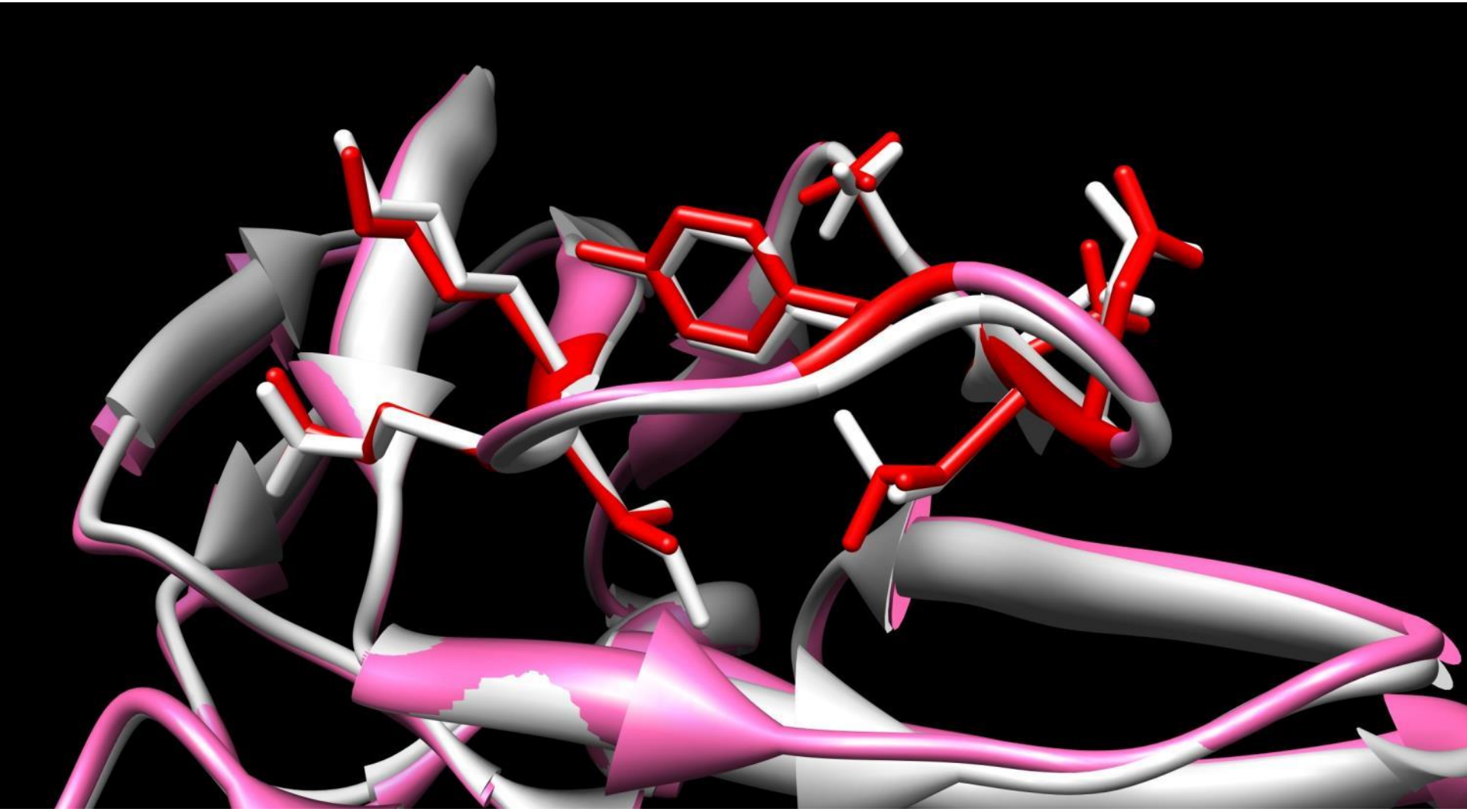
9. Mtb cdd (PDB:3IJF, white), *M. leprae* cdd (3R2N, red/pink)
Sequence identity 57%, PS_{APF} 92%



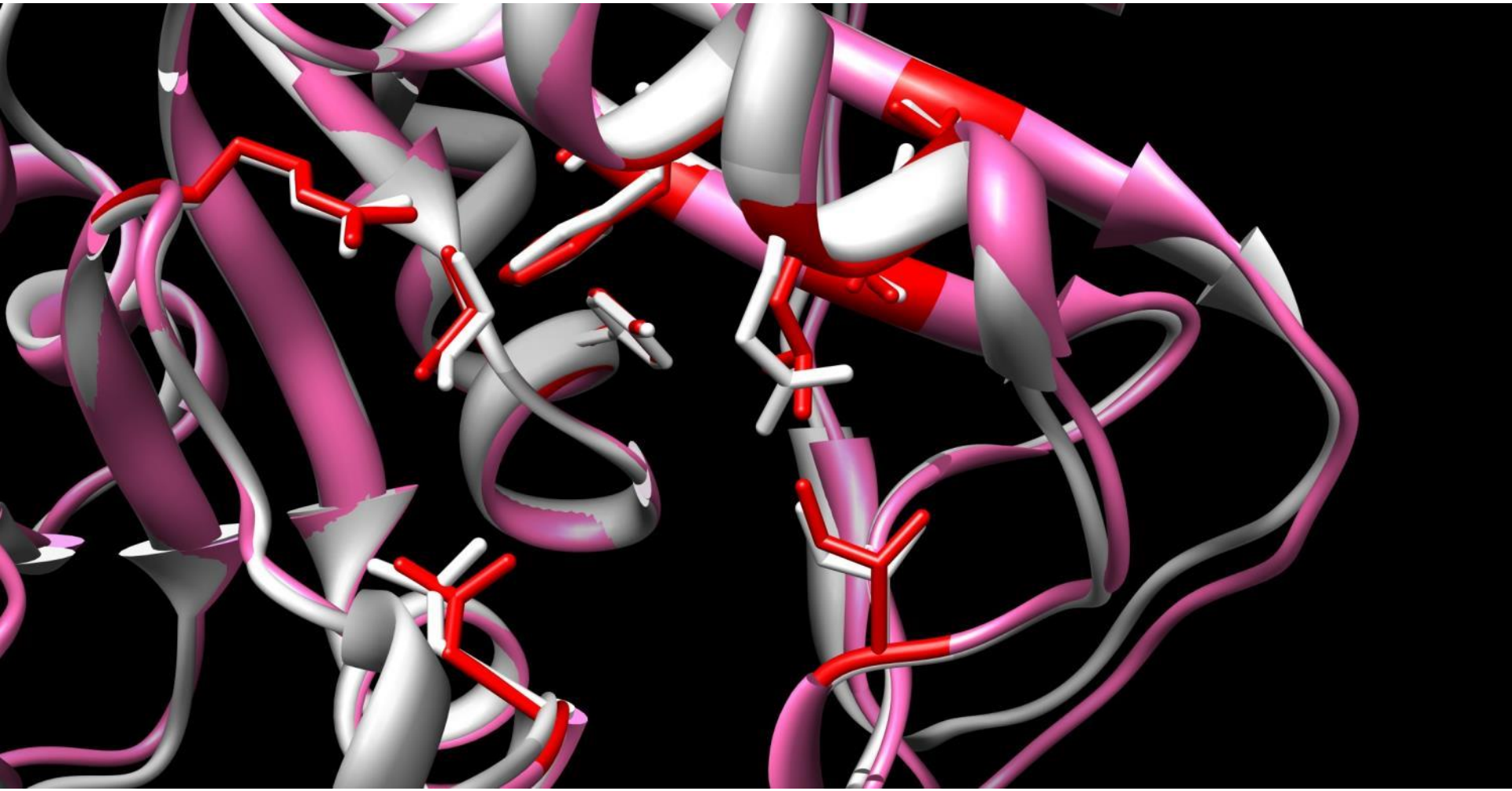
10. Mtb gabG4 (PDB:3V1T, white), *M. smegmatis* fabG4 (3U0B, red/pink)
Sequence identity 84%, PS_{APF} 92%



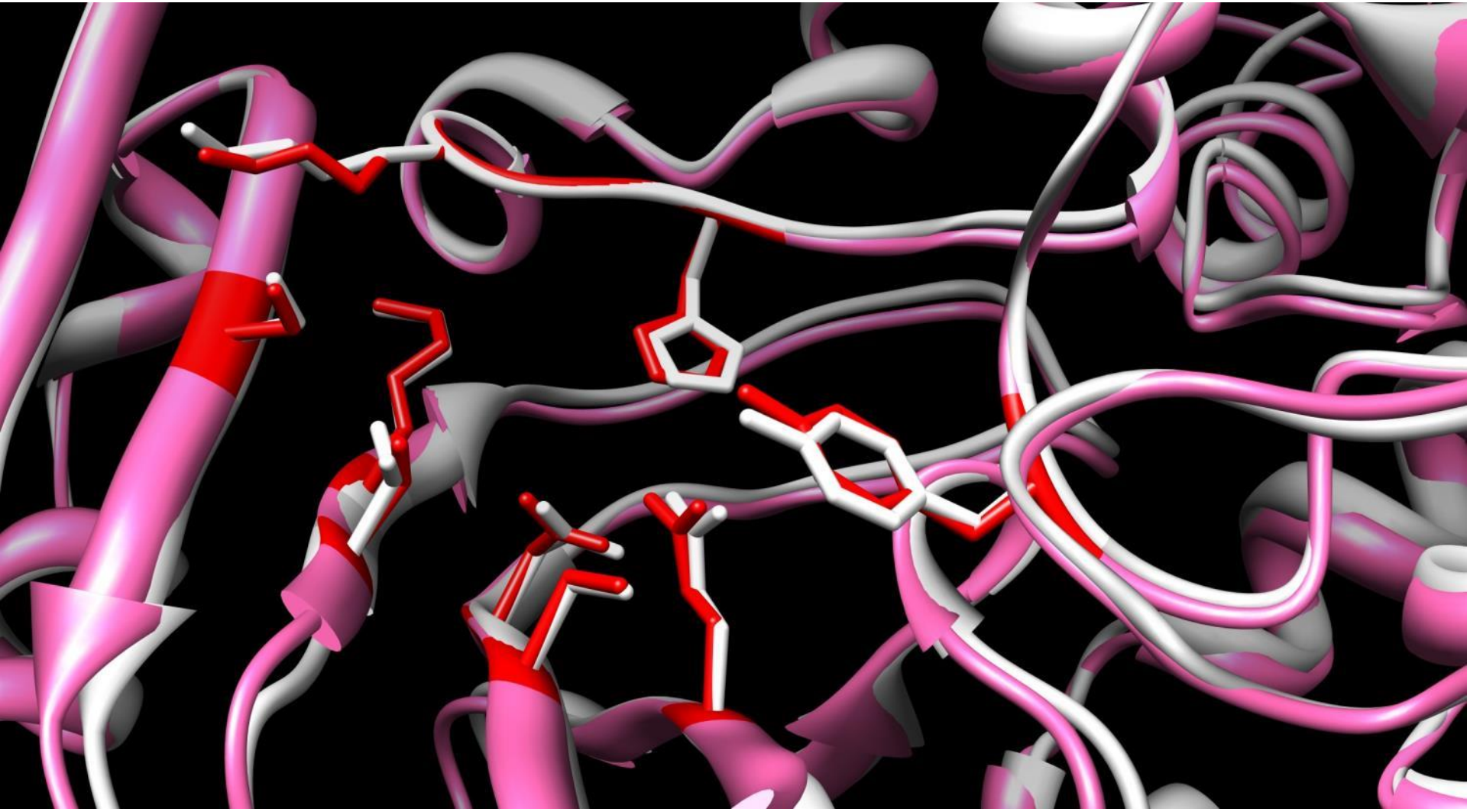
11. Mtb dut (PDB:1MQ7, white), *M. abscessus* dut (4GK6, red/pink)
Sequence identity 81%, PS_{APF} 90%



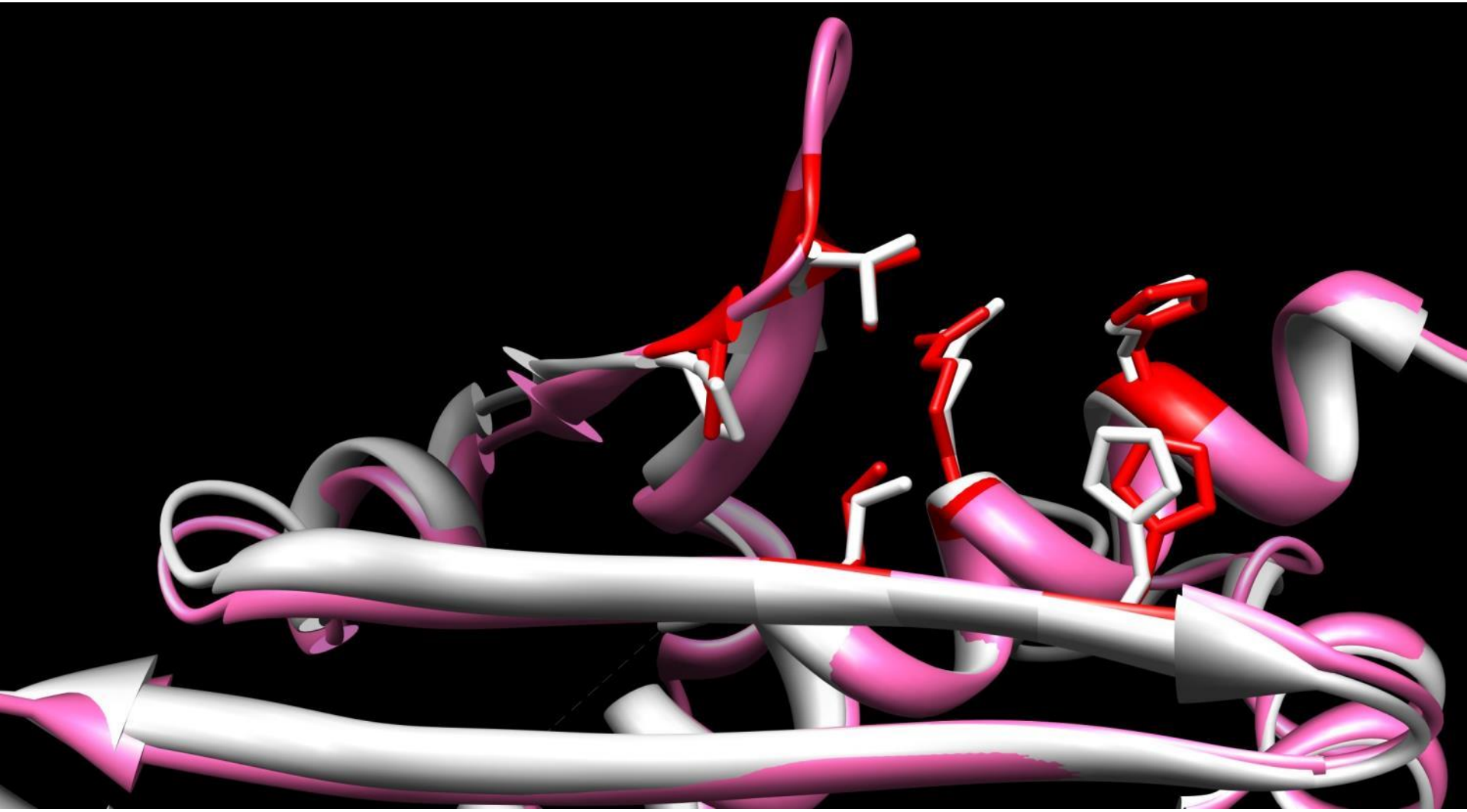
12. Mtb folA (PDB:1DG8, white), *M. avium* folA (2W3V, red/pink)
Sequence identity 70%, PS_{APF} 90%



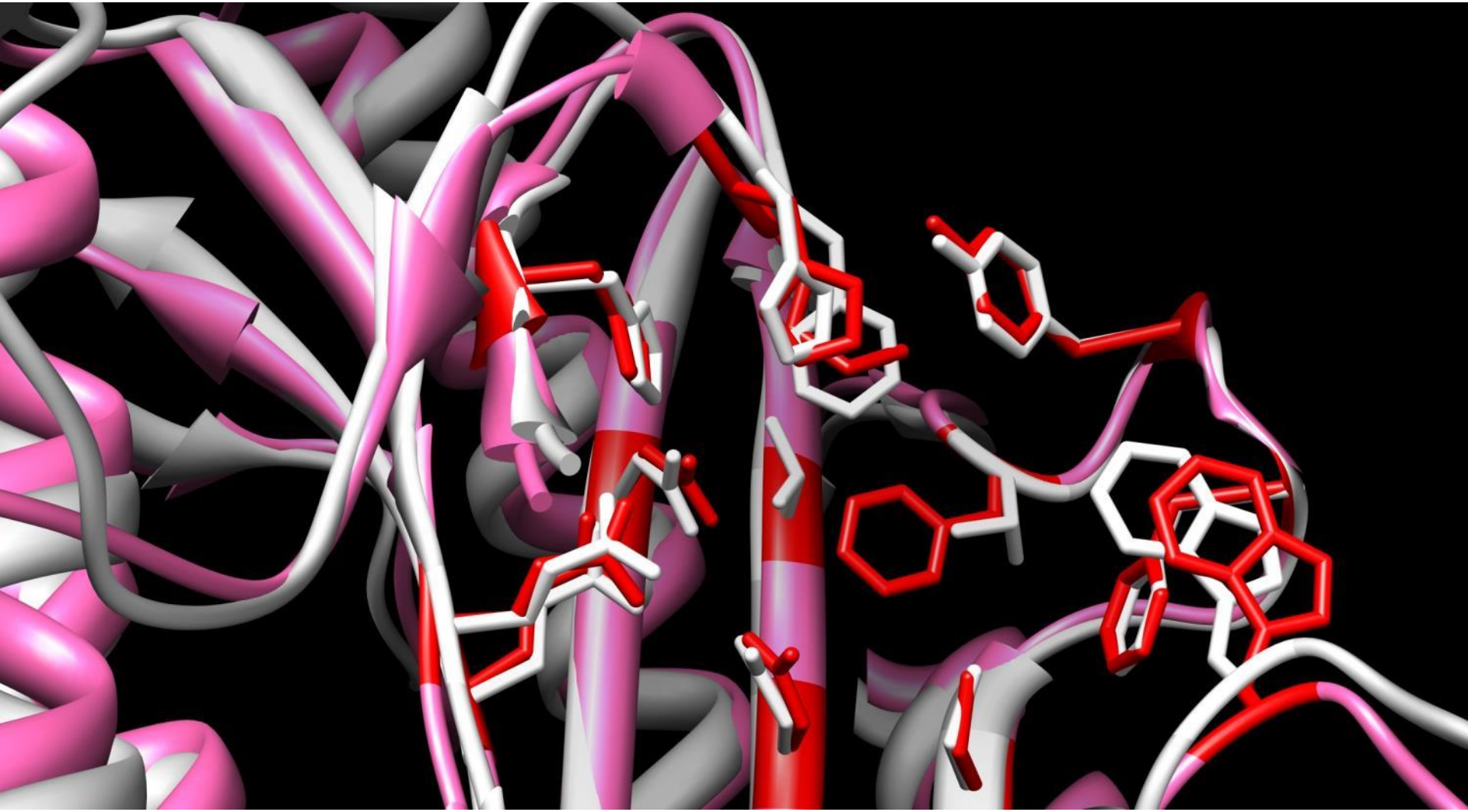
13. Mtb dprE1 (PDB:4FEH, white), *M. smegmatis* MSMEG_6382 (4AUT, red/pink)
Sequence identity 84%, PS_{APF} 89%



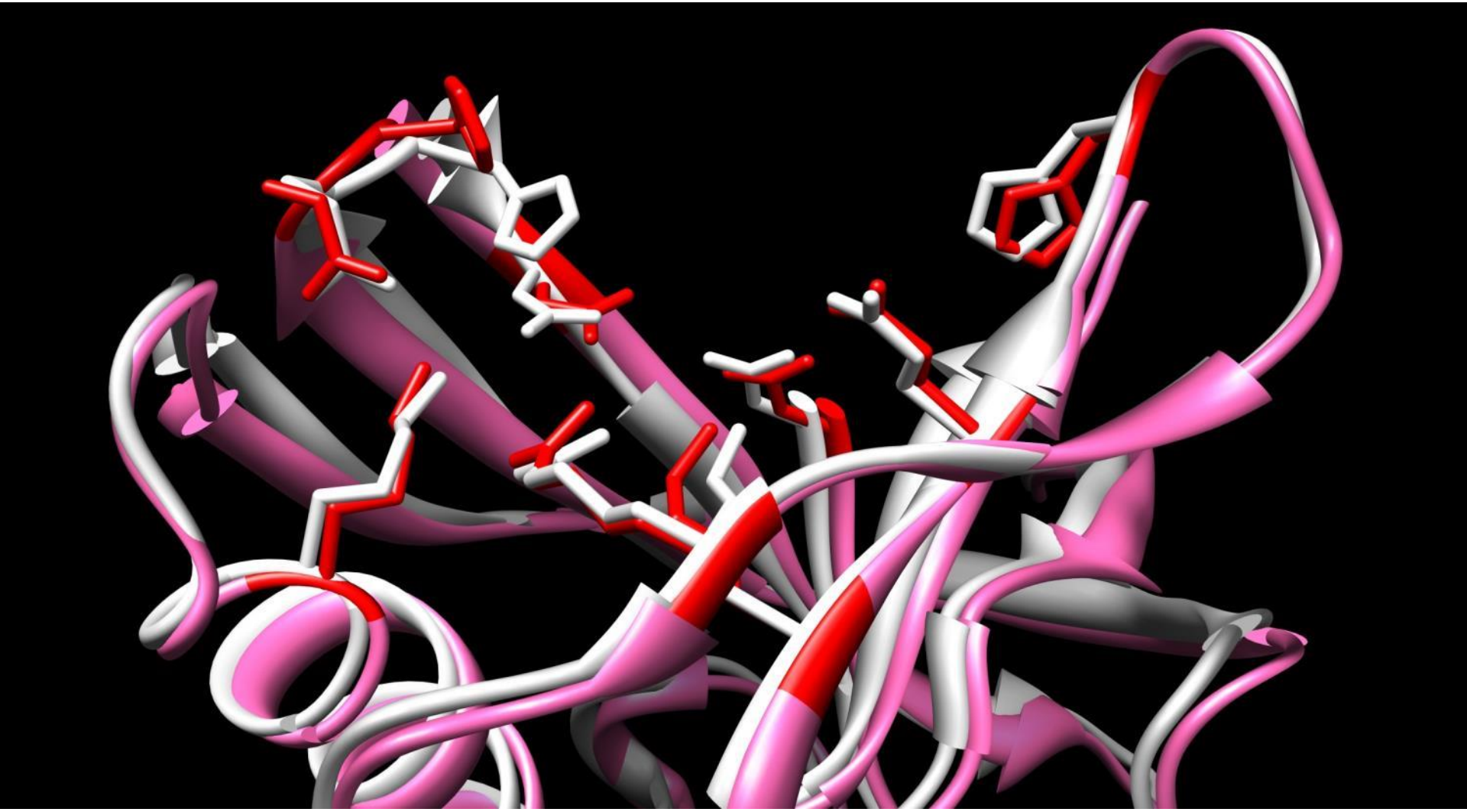
14. Mtb acpS (PDB:3H7Q, white), *M. smegmatis* acpS (3GWM, red/pink)
Sequence identity 86%, PS_{APF} 89%



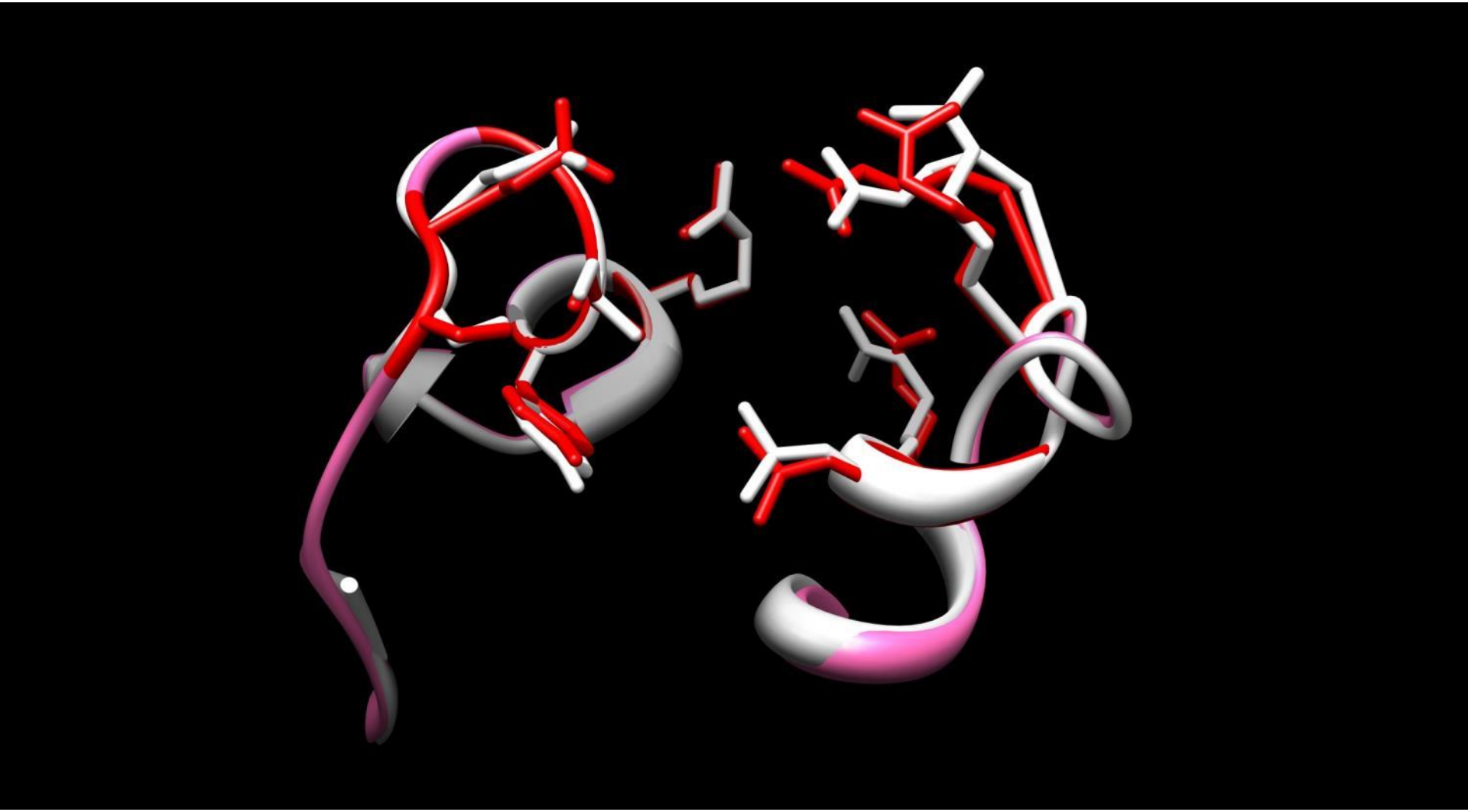
15. Mtb map (PDB:1YJ3, white), *M. abscessus* MAB_3782c (3TAV, red/pink)
Sequence identity 26%, PS_{APF} 86%



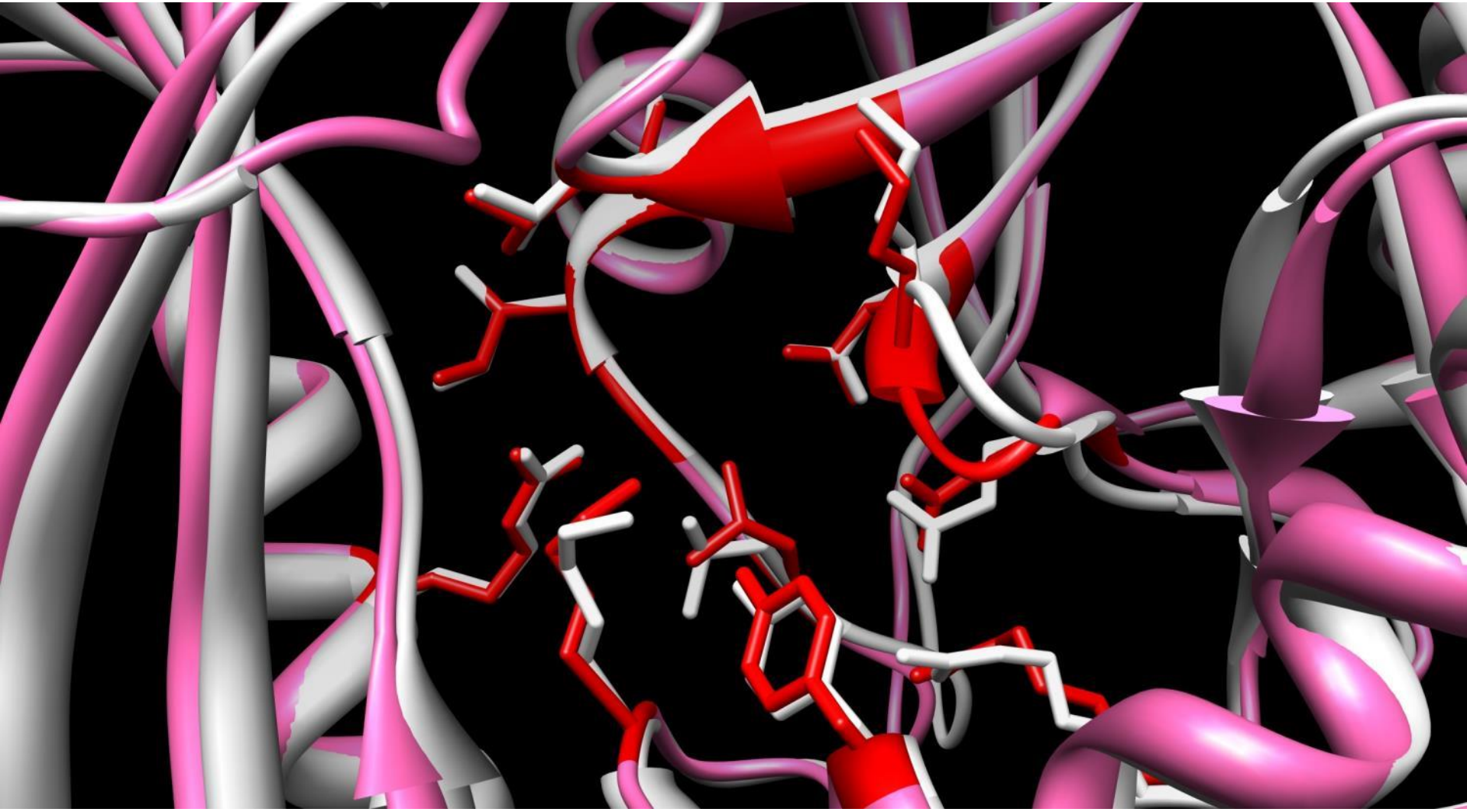
16. Mtb ppa (PDB:1SXV, white), *M. leprae* ppa (4ECP, red/pink)
Sequence identity 90%, PS_{APF} 85%



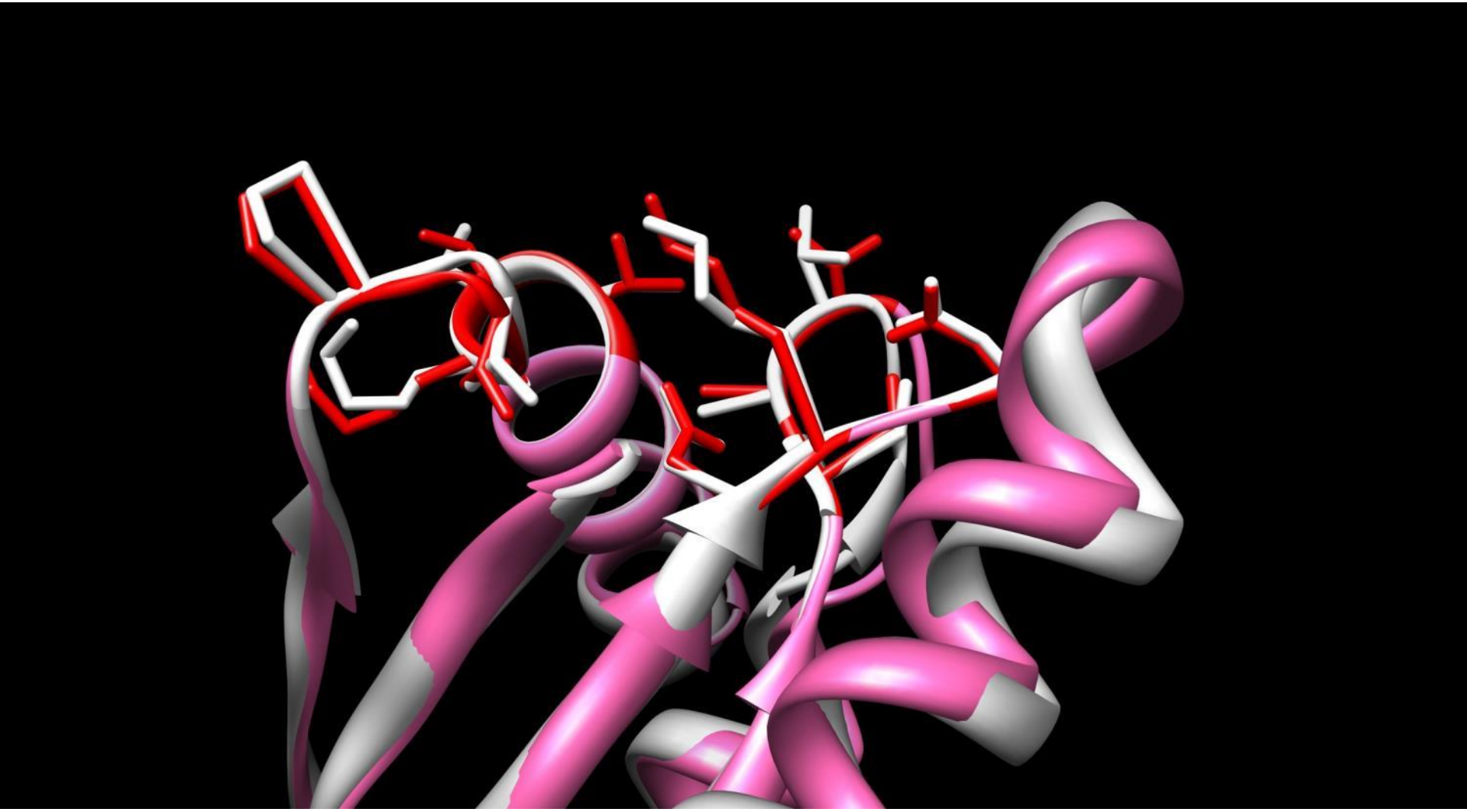
17. Mtb eis (PDB:3R1K, white), *M. smegmatis* eis (3SXN, red/pink)
Sequence identity 58%, PS_{APF} 85%



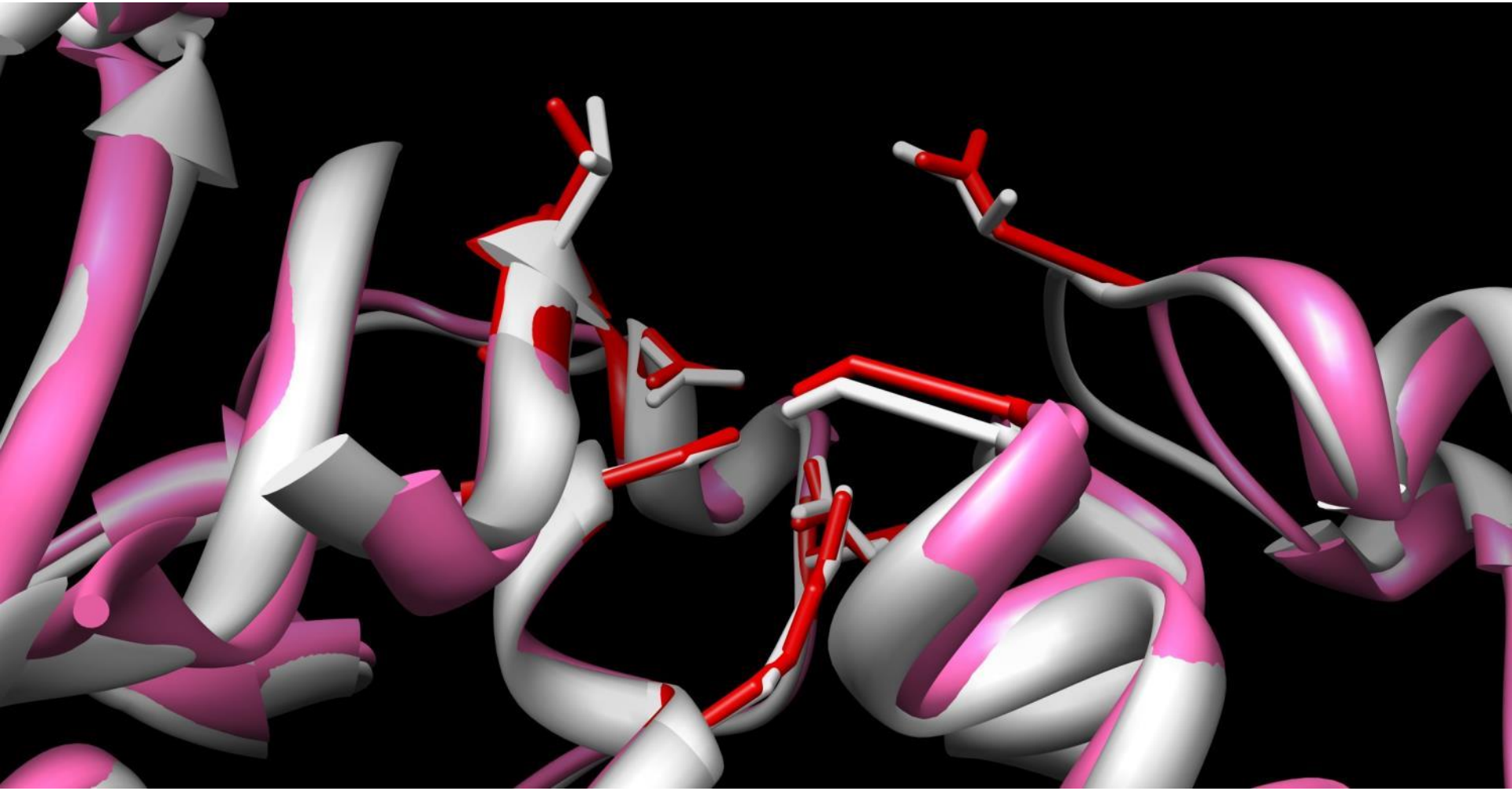
18. Mtb ilvE (PDB:3HT5, white), *M. smegmatis* ilvE (3DTF, red/pink)
Sequence identity 85%, PS_{APF} 84%



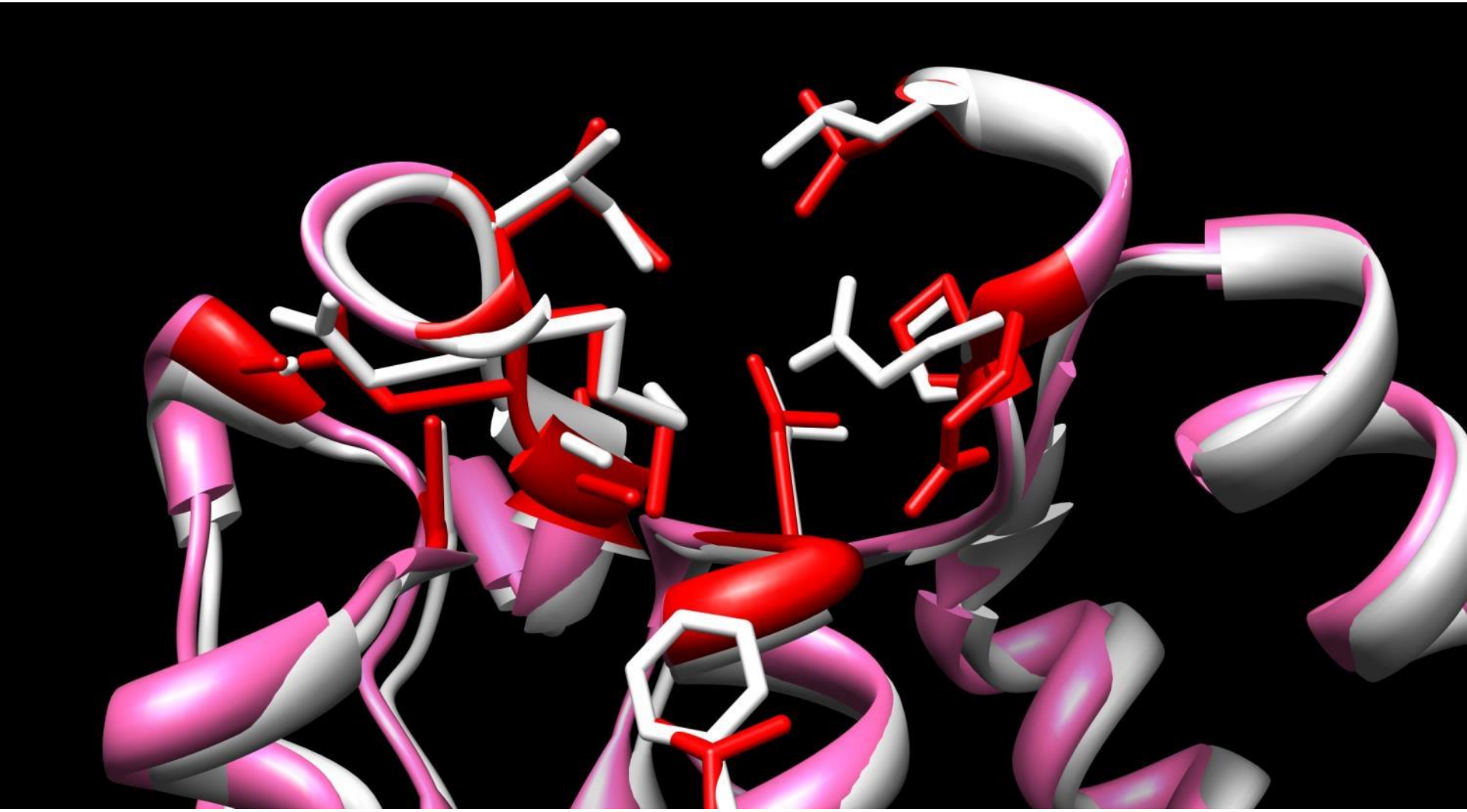
19. Mtb Rv1486 (PDB:3MD0, white), *M. smegmatis* MSMEG_3160 (3NXS, red/pink)
Sequence identity 80%, PS_{APF} 83%



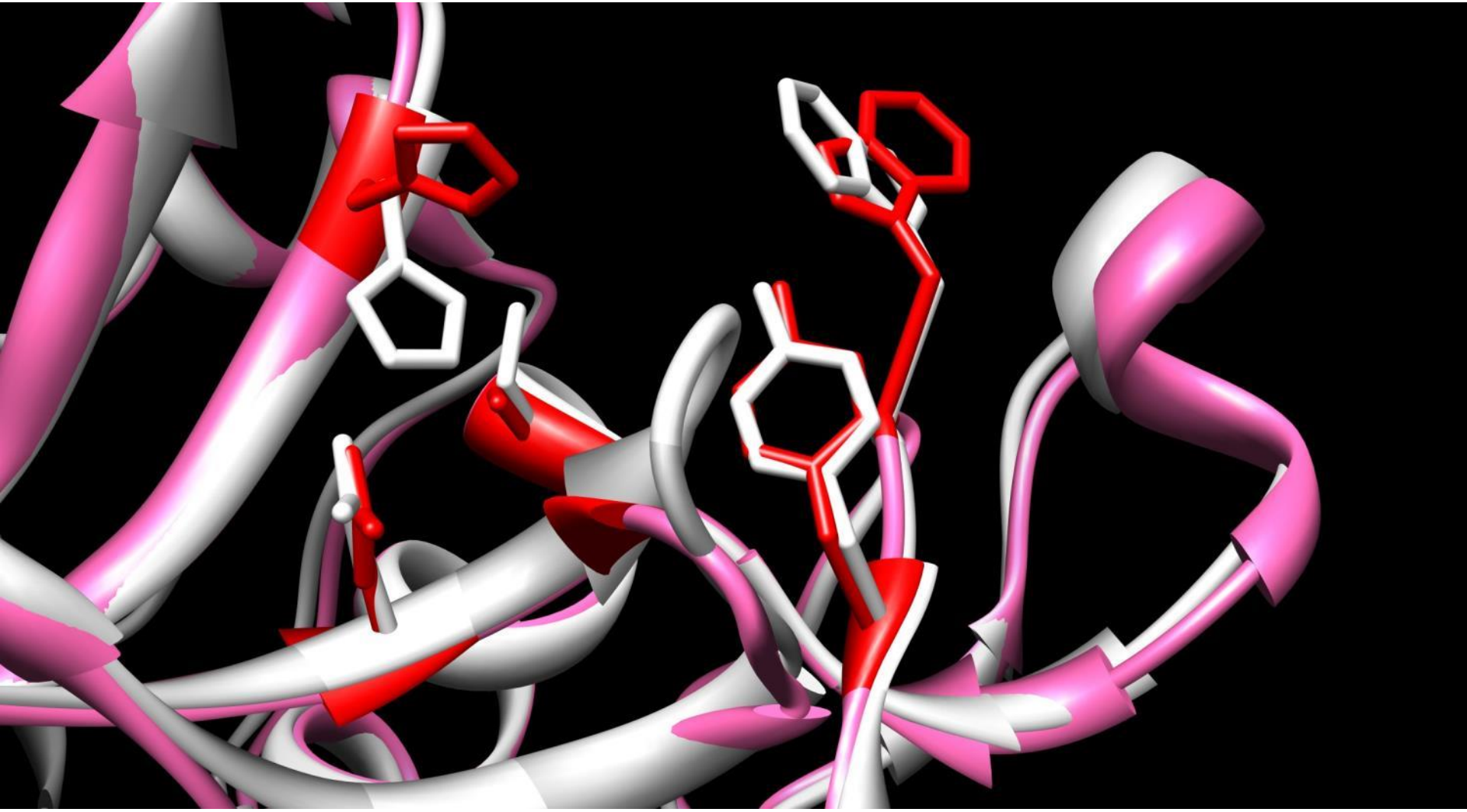
20. Mtb blaA (PDB:2GDN, white), *M. fortuitum* blaF (2CC1, red/pink)
Sequence identity 39%, PS_{APF} 82%



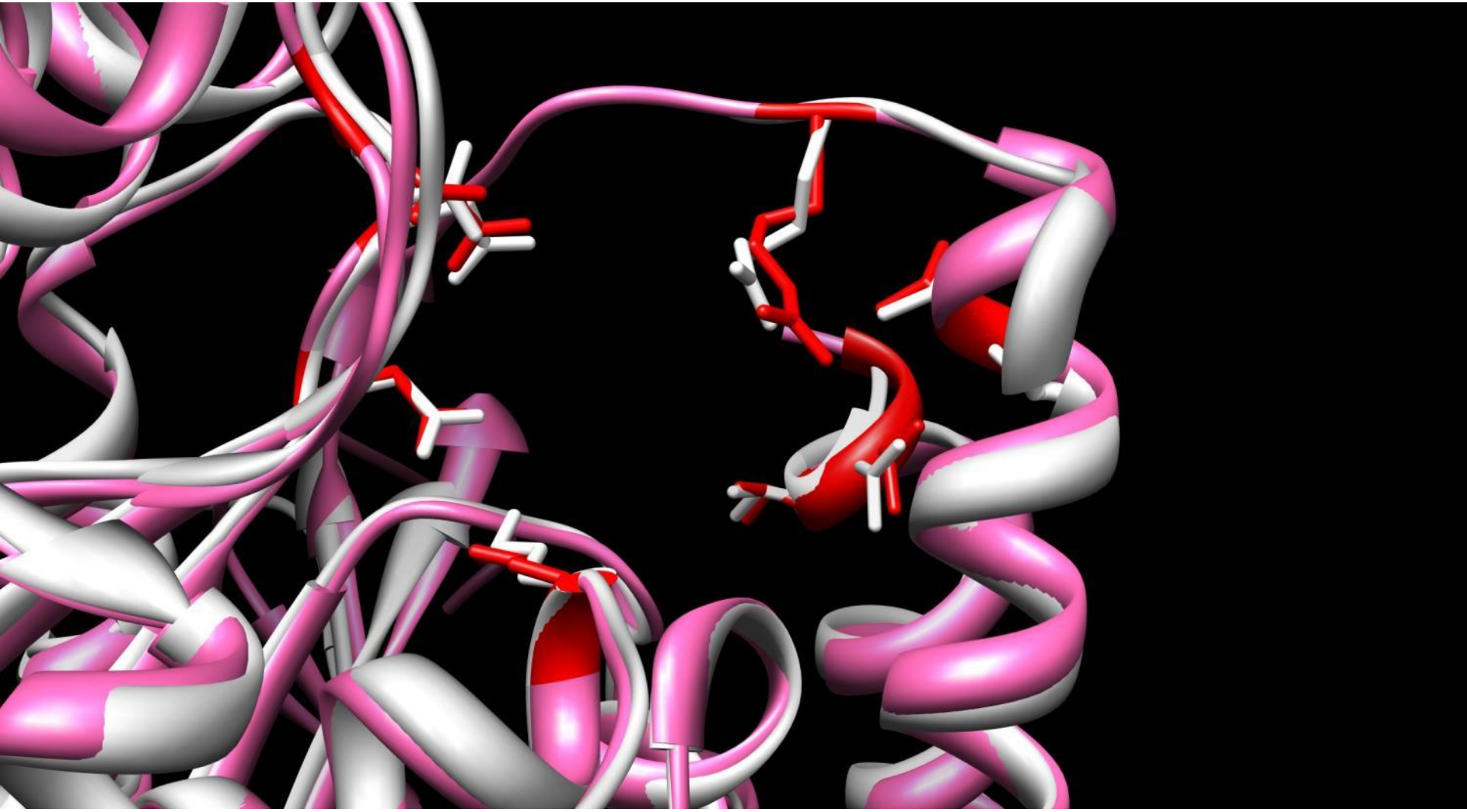
21. Mtb echA8 (PDB:3H81, white), *M. smegmatis* echA8 (3MOY, red/pink)
Sequence identity 61%, PS_{APF} 79%



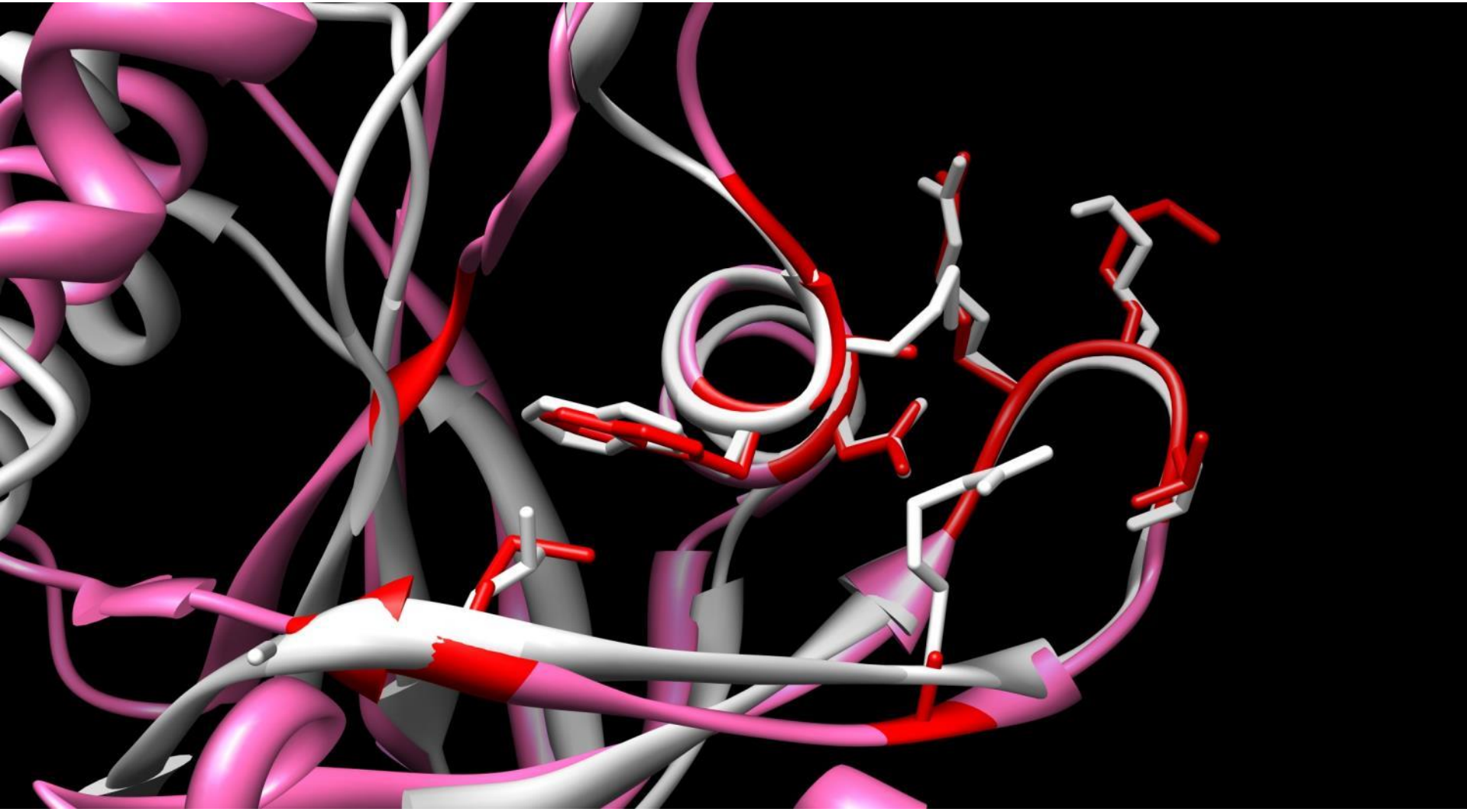
22. Mtb ripA (PDB:3PBI, white), *M. paratuberculosis* MAP_1204 (3I86, red/pink)
Sequence identity 78%, PS_{APF} 71%



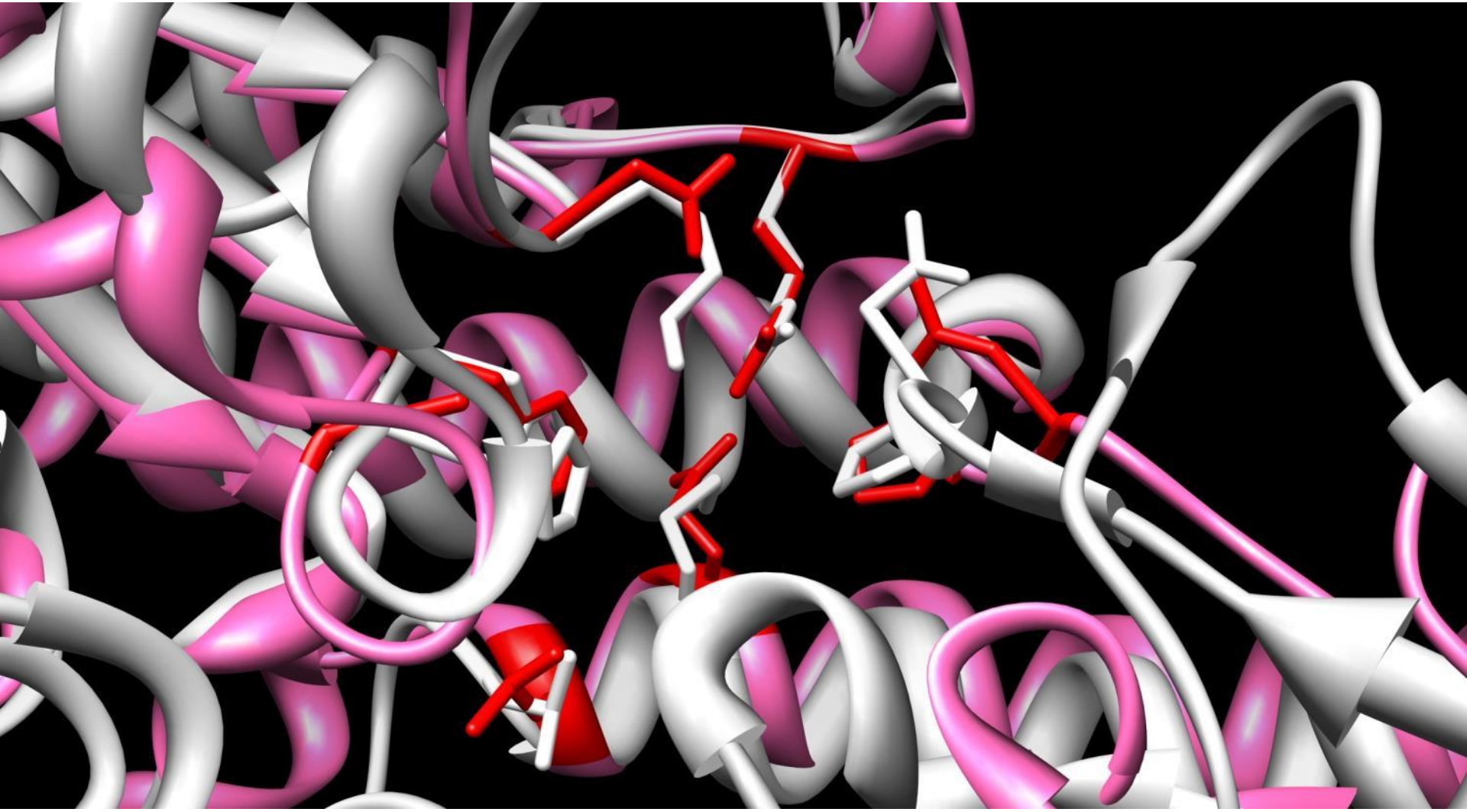
23. Mtb gpgS (PDB:3E25, white), *M. paratuberculosis* MAP_2569c (3CKQ, red/pink)
Sequence identity 82%, PS_{APF} 71%



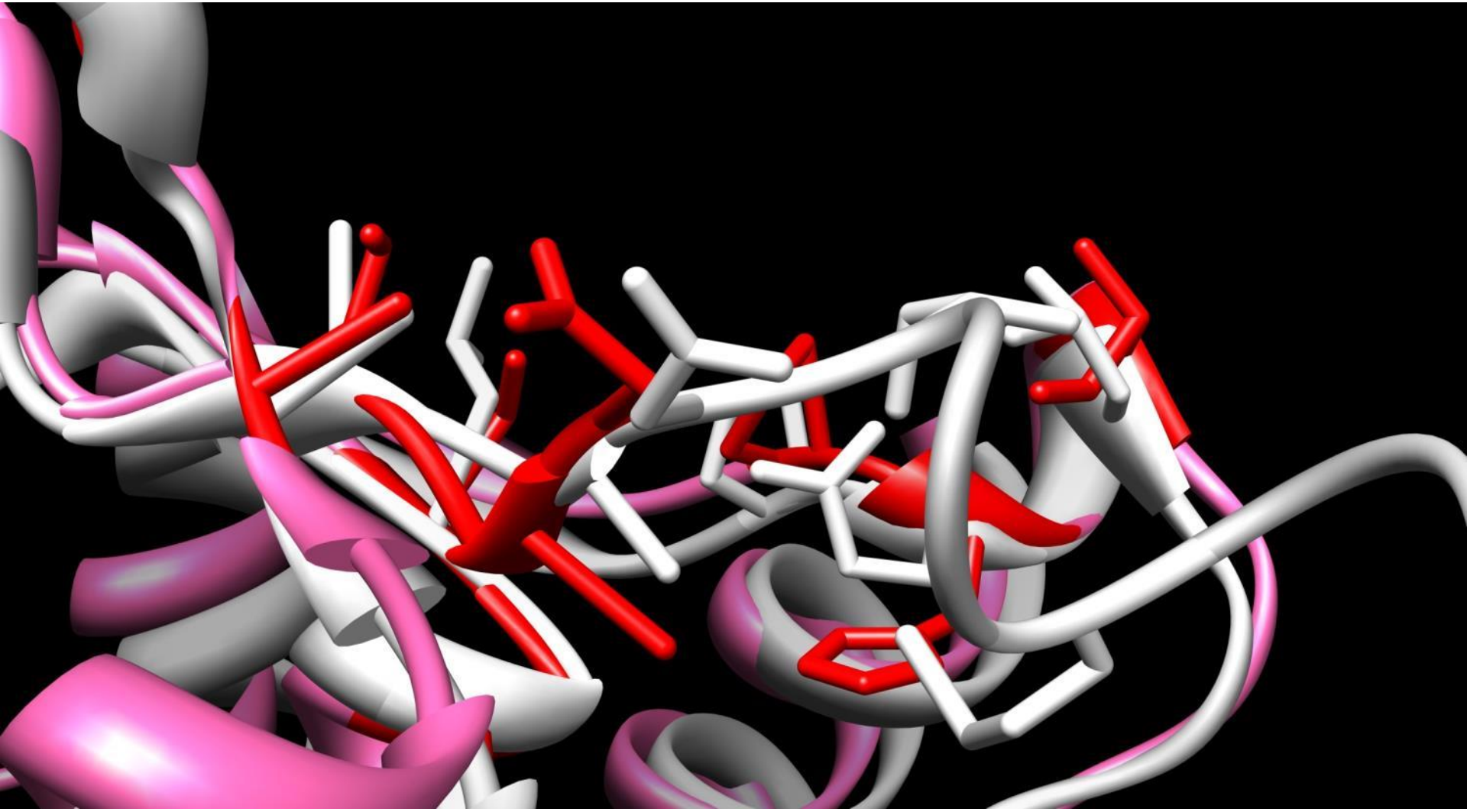
24. Mtb ddn (PDB:3R5L, white), *M. smegmatis* MSMEG_3356 (3H96, red/pink)
Sequence identity 36%, PS_{APF} 69%



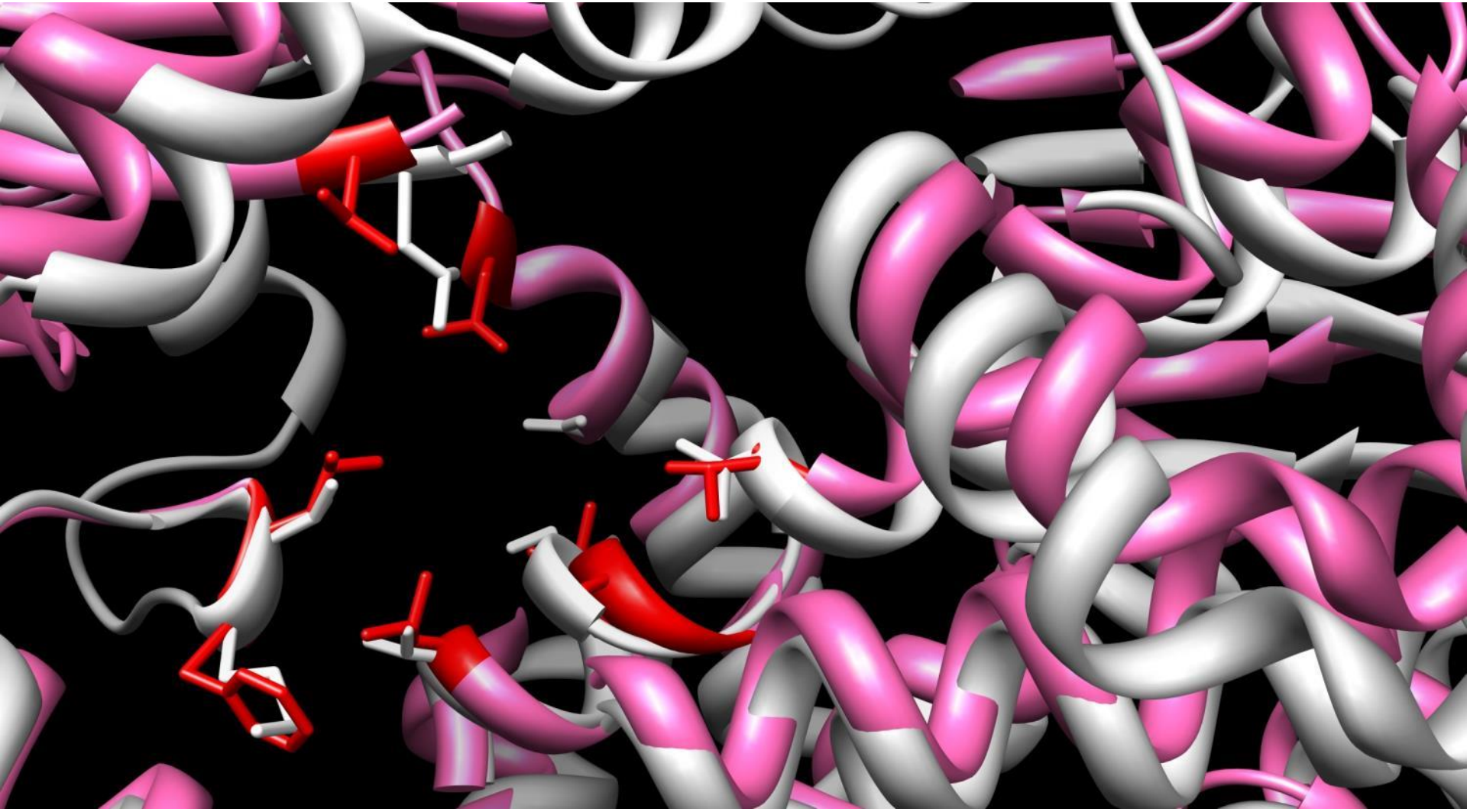
25. Mtb ald (PDB:2VHV, white), *M. smegmatis* pntAa (3P2Y, red/pink)
Sequence identity 32%, PS_{APF} 65%



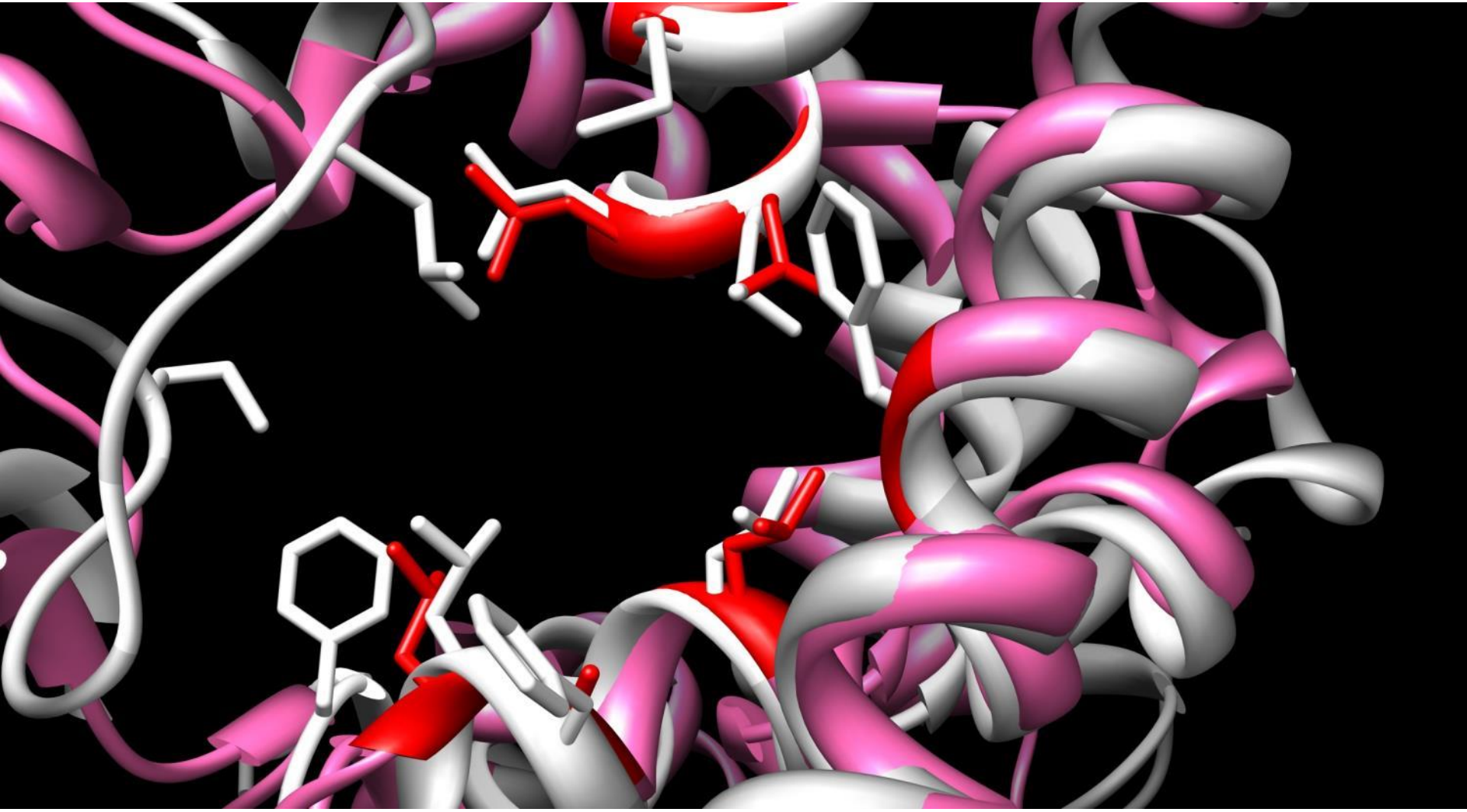
26. Mtb echA8 (PDB:3H81, white), *M. paratuberculosis* MAP_2398 (3TLF, red/pink)
Sequence identity 30%, PS_{APF} 57%



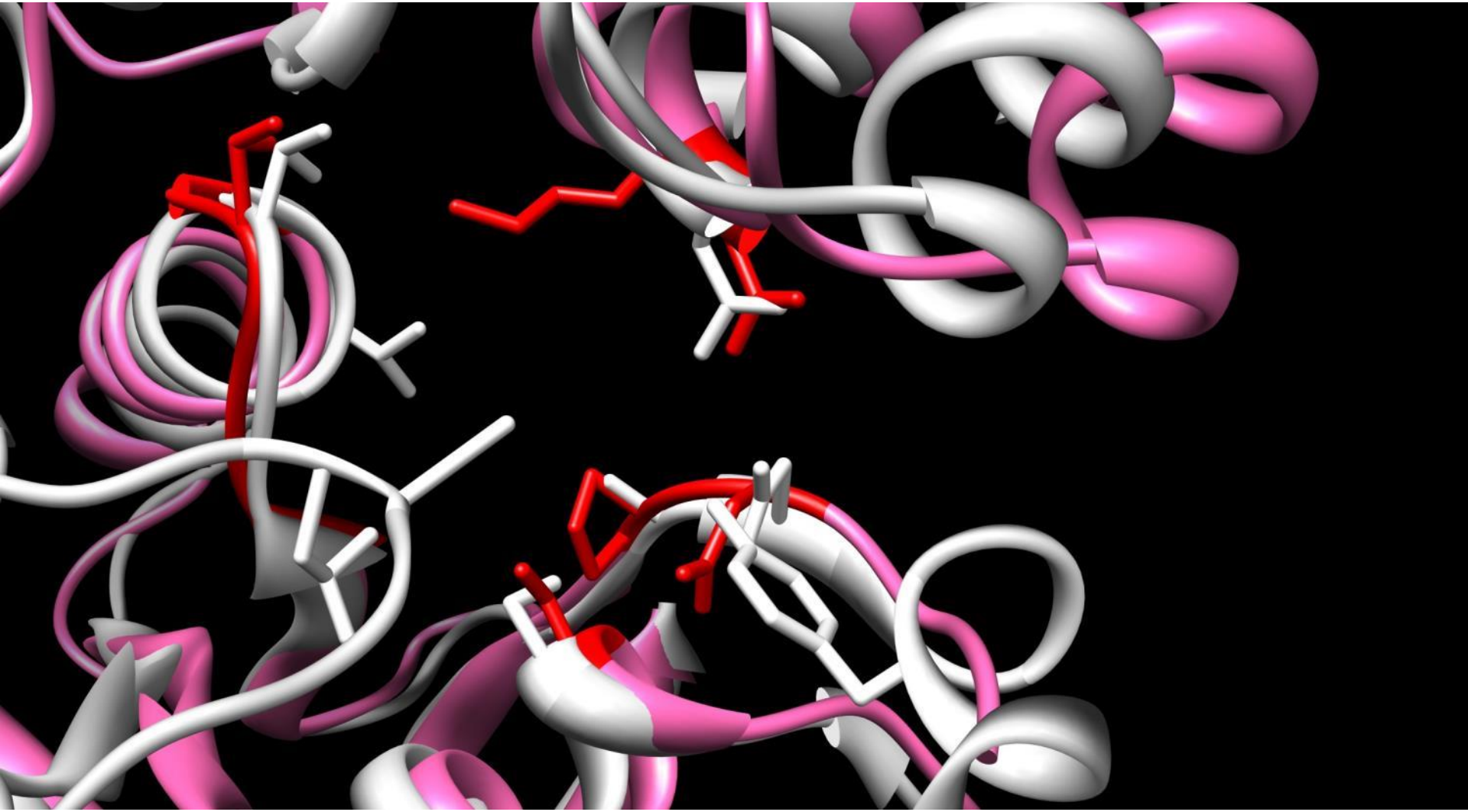
27. Mtb cyp130 (PDB:2UUQ, white), *M. smegmatis* cyp123 (3R9B, red/pink)
Sequence identity 31%, PS_{APF} 57%



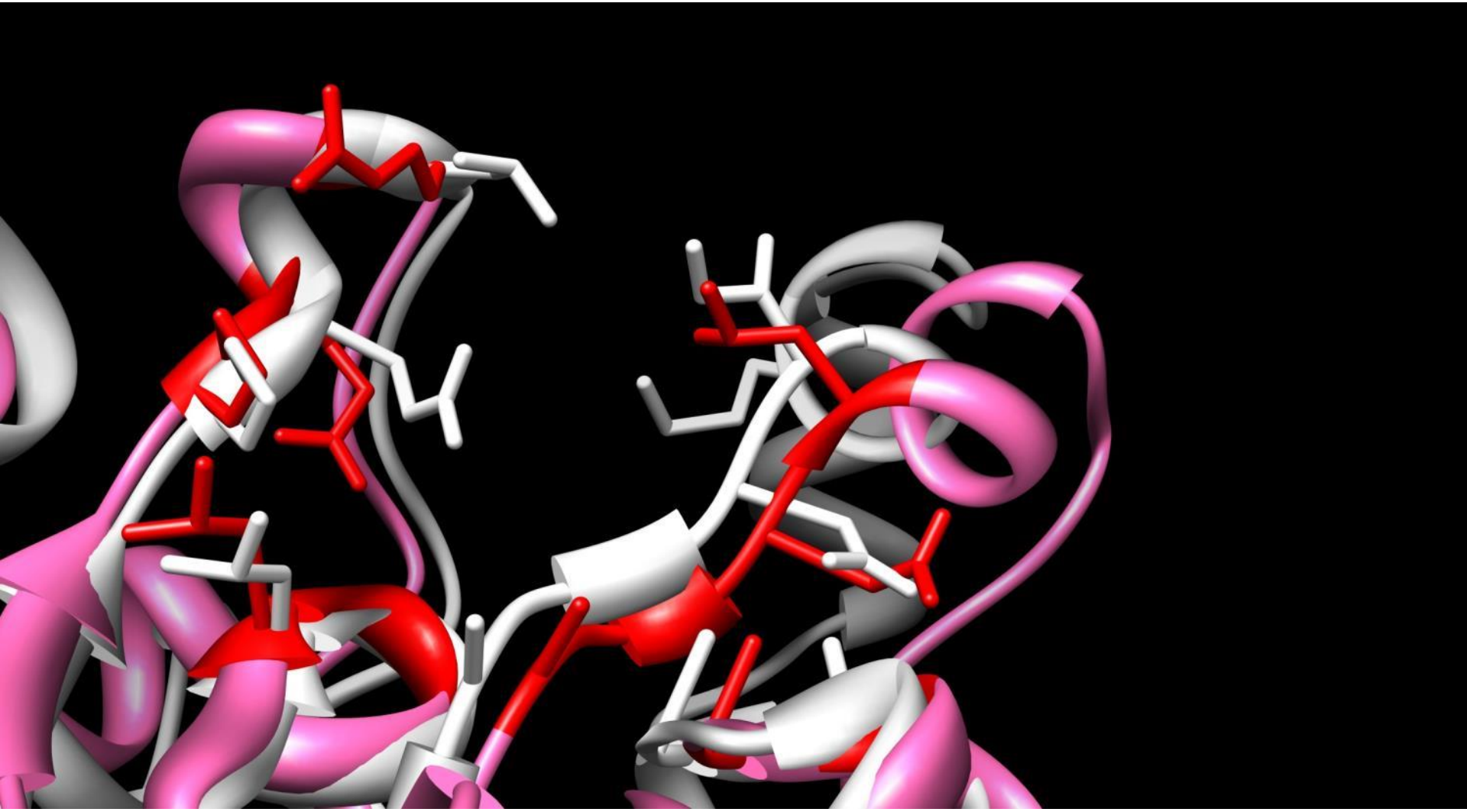
28. Mtb cyp142 (PDB:2XKR, white), *M. smegmatis* cyp123 (3R9B, red/pink)
Sequence identity 35%, PS_{APF} 56%



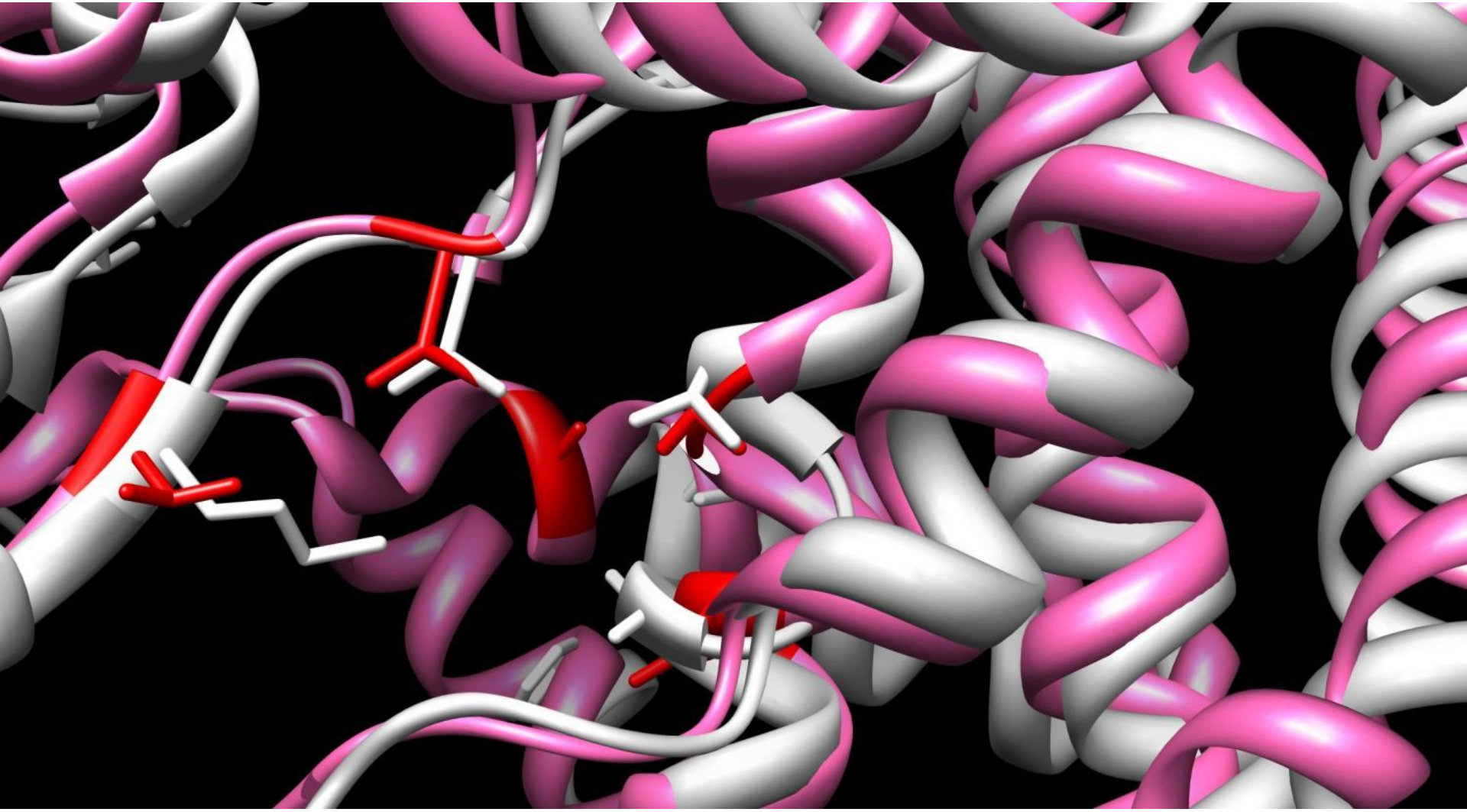
29. Mtb cysM (PDB:3DKI, white), *M. marinum* cysK1 (3RR2, red/pink)
Sequence identity 38%, PS_{APF} 55%



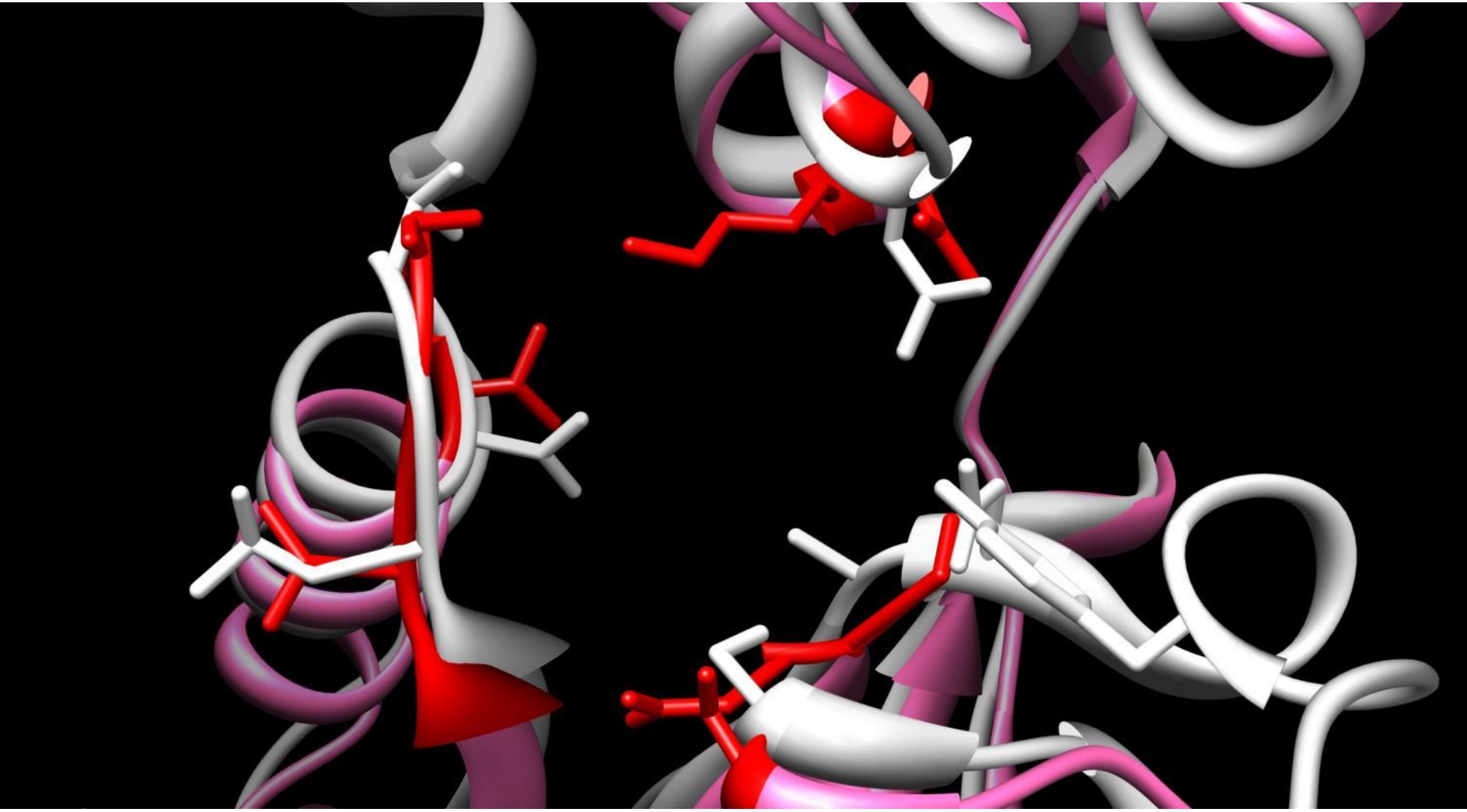
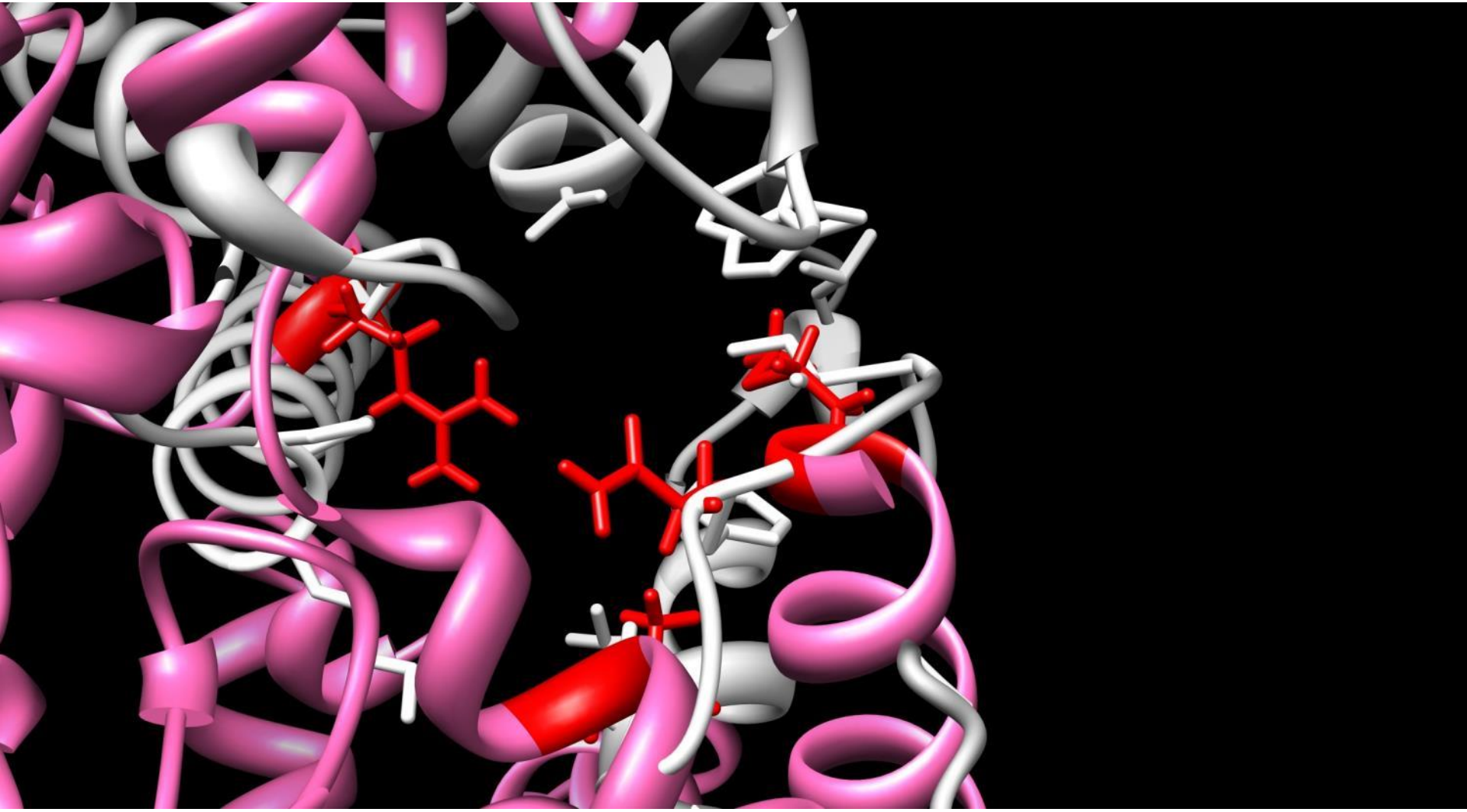
30. Mtb echA8 (PDB:3H81, white), *M. avium* MAV_2597 (3R0O, red/pink)
Sequence identity 37%, PS_{APF} 49%



31. Mtb cyp124 (PDB:2WM5, white), *M. smegmatis* cyp123 (3R9B, red/pink)
Sequence identity 32%, PS_{APF} 42%



32. Mtb cysM (PDB:3DKI, white), *M. ulcerans* cysK1 (4I1Y, red/pink)
Sequence identity 38%, PS_{APF} 39%



33. Mtb cyp125 (PDB:2X5L, white), *M. smegmatis* cyp123 (3R9B, red/pink)
Sequence identity 25%, PS_{APF} 23%