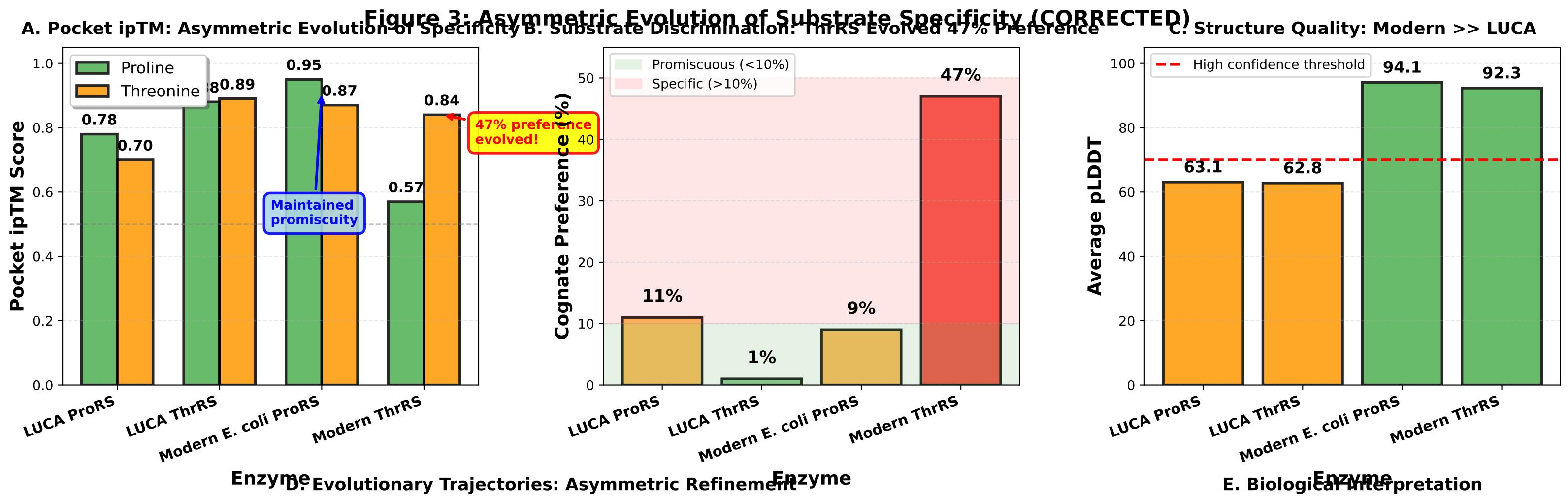
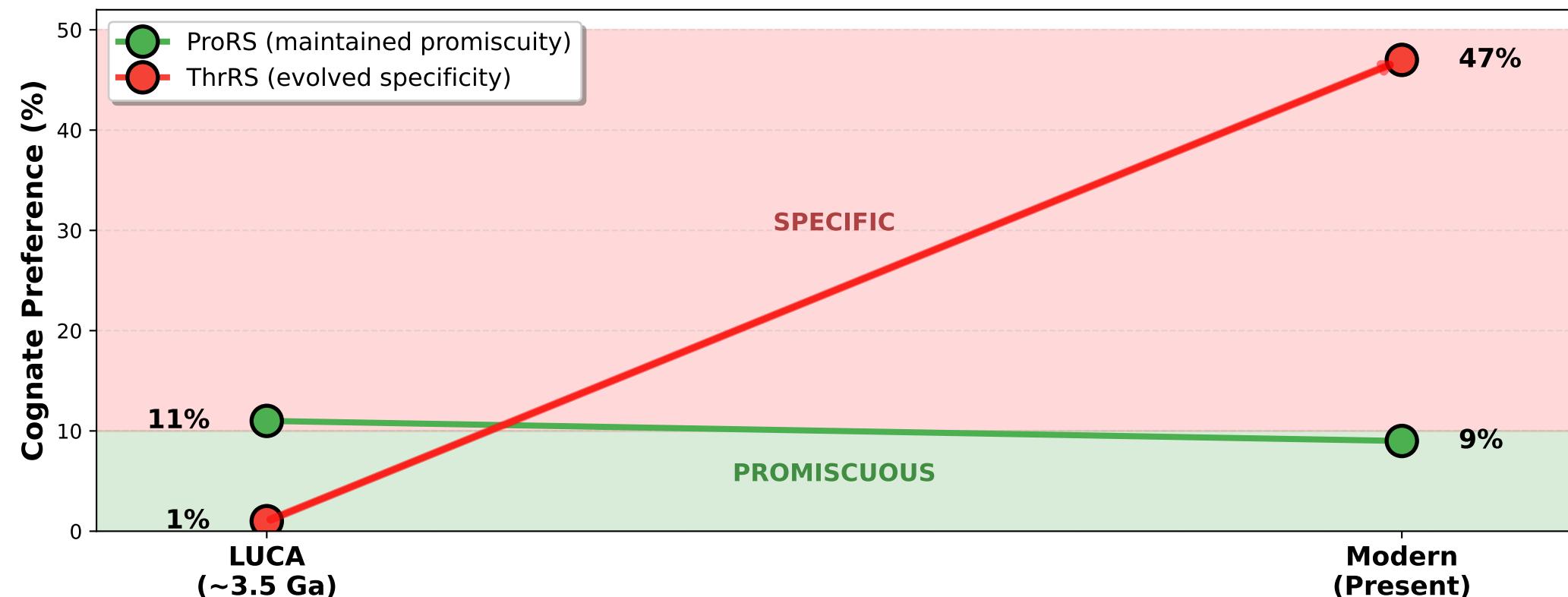


Figure 3: Asymmetric Evolution of Substrate Specificity (CORRECTED)



D. Evolutionary Trajectories: Asymmetric Refinement



ASYMMETRIC EVOLUTION:

LUCA (Ancestral):

- ProRS: 11% preference (mild)
- ThrRS: 1% preference (promiscuous)
- Both relatively promiscuous

Modern:

- ProRS: 9% preference (MAINTAINED)
- ThrRS: 47% preference (EVOLVED!)
- Divergent fidelity strategies

KEY FINDINGS:

1. ProRS MAINTAINED promiscuity
→ Likely due to editing domain compensation (3.2x preference for Thr-tRNA^{Pro})
2. ThrRS EVOLVED specificity
→ 47-fold increase in preference
→ May lack effective editing
3. Differential selection pressure
→ Thr→Pro errors more deleterious?
→ ProRS can tolerate catalytic promiscuity with editing backup

BIOLOGICAL SIGNIFICANCE:
ProRS uses TWO-STAGE fidelity:

- 1) Catalytic promiscuity (9%)
- 2) Editing specificity (320%)
- = Overall high fidelity

ThrRS evolved SINGLE-STAGE:

- High catalytic specificity (47%)
- Less editing dependency