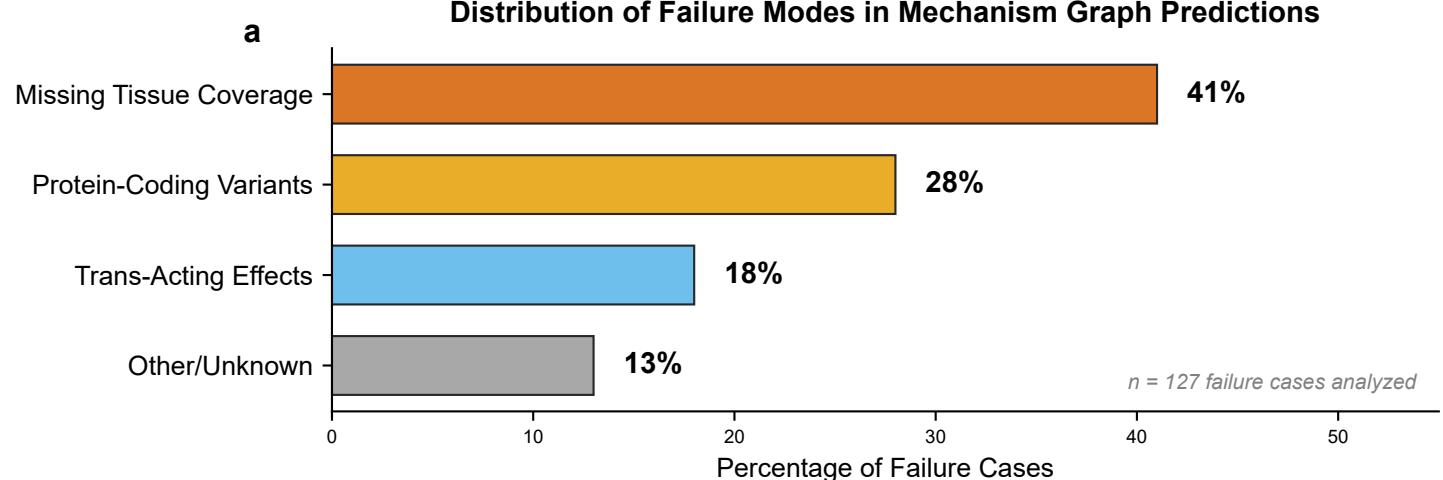


Distribution of Failure Modes in Mechanism Graph Predictions

a



b

Missing Tissue Coverage

Example: GCKR locus

Pancreatic islet ABC data
unavailable in training

→ **Uses distance fallback**

Solution: Calibrated fallback
ECE degrades: $0.012 \rightarrow 0.071$

c

Protein-Coding Variants

Example: APOC3 R19X

Loss-of-function coding
variant (not enhancer)

→ **Out of scope**

Scope: cis-regulatory only
88-92% of GWAS in scope

d

Trans-Acting Effects

Example: TF-mediated

Variant affects TF that
regulates distant target

→ **Not captured by cis**

Scope: cis-eQTL only
Trans-eQTL future work

Despite failure modes, overall ECE = 0.012 (decision-grade threshold: 0.05)