Protein Structure Explorer: Mutation Analysis of 1AKE

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1. Research question & motivation

Adenylate kinase (**1AKE**) is a benchmark model for studying conformational switching in energy-metabolism enzymes.
Goal: Quantify how single-point mutations alter 1AKE's structural stability.
Why it matters: insights guide protein-engineering, inhibitor design and the interpretation of disease-linked variants.

2. Methods

- **Data source** – crystal structure downloaded from the RCSB PDB (mmCIF format).
- **Parsing** – BioPython (PDB / MMCIF parsers) for coordinate extraction.
- **In-silico mutagenesis** – side-chain replaced and rotated by a fixed 45 ° about the Cα atom (fast, geometry-only).
- **Metrics** –
    - **RMSD**: Cα-based superposition of wild-type vs. mutant;
    - **COM shift**: Euclidean distance between mass centres of Cα atoms.

3. Mutation panel

Fifteen mutants spanning functional / structural categories:

#	WT res	Pos.	Mut	Category
1	K	13	A	Catalytic neutralisation
2	R	36	A	Catalytic neutralisation
3	A	37	G	Flexibility ↑
4	I	53	P	Fold-kink probe
5	L	82	D	Hydrophobe → charged
6	D	93	N	Charge removal
7	R	119	E	Charge swap
8	F	120	A	Hydrophobe → Ala

9	G	122	P	Proline rigidification
10	L	134	P	Helix breaker
11	V	148	W	Bulky hydrophobe → Trp
12	R	156	A	Catalytic neutralisation
13	D	158	N	Charge removal
14	Y	171	F	Aromatic H-bond loss
15	T	175	A	Ser/Thr scan

4. Key results

Mutation	RMSD (Å)	COM shift (Å)	Comment
R36A	**3.27**	0.005	largest global distortion
K13A	2.76	0.003	catalytic Lys removal
L134P	2.55	0.003	helix kink introduced
mean (15)	1.78	0.002	most mutants localised

- **RMSD plot –** broad spread: 0.0 Å (G122P) → 3.3 Å (R36A).
- **COM shift plot –** ≤ 0.005 Å for all mutants → global fold largely retained.

(Figures included in the PDF: mutation_rmsd.png & mutation_com_shift.png.)

5. Limitations

- Geometry-only mutagenesis; no energy minimisation or solvation.
- Insertion codes and long chain identifiers not handled.
- Metrics omit side-chain clashes and functional assays.

6. Future work

- Integrate molecular-dynamics minimisation for realistic energetics.
- Generalise residue-mapping (PDB ⇄ UniProt) with insertion codes.
- Apply workflow to additional kinases; correlate with enzymatic activity.