Supporting information for manuscript titled "Mechanistic Insights into R776H Mediated Activation of Epidermal Growth Factor Receptor (EGFR) Kinase"

Zheng Ruan[†,‡] and Natarajan Kannan[*,†]

Department of Biochemistry & Molecular Biology, University of Georgia, Athens, GA, USA, and Institute of Bioinformatics, University of Georgia, Athens, GA, USA

E-mail: kannan@bmb.uga.edu

Supporting Information

Supporting Information Available: Figure S1, Figure S2, Figure S3, Figure S4, Figure S5, Figure S6, Table S1, Table S2. This material is available free of charge via the Internet at http://pubs.acs.org.

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[*] To whom correspondence should be addressed

[†] Department of Biochemistry & Molecular Biology, University of Georgia, Athens, GA, USA

[‡] Institute of Bioinformatics, University of Georgia, Athens, GA, USA

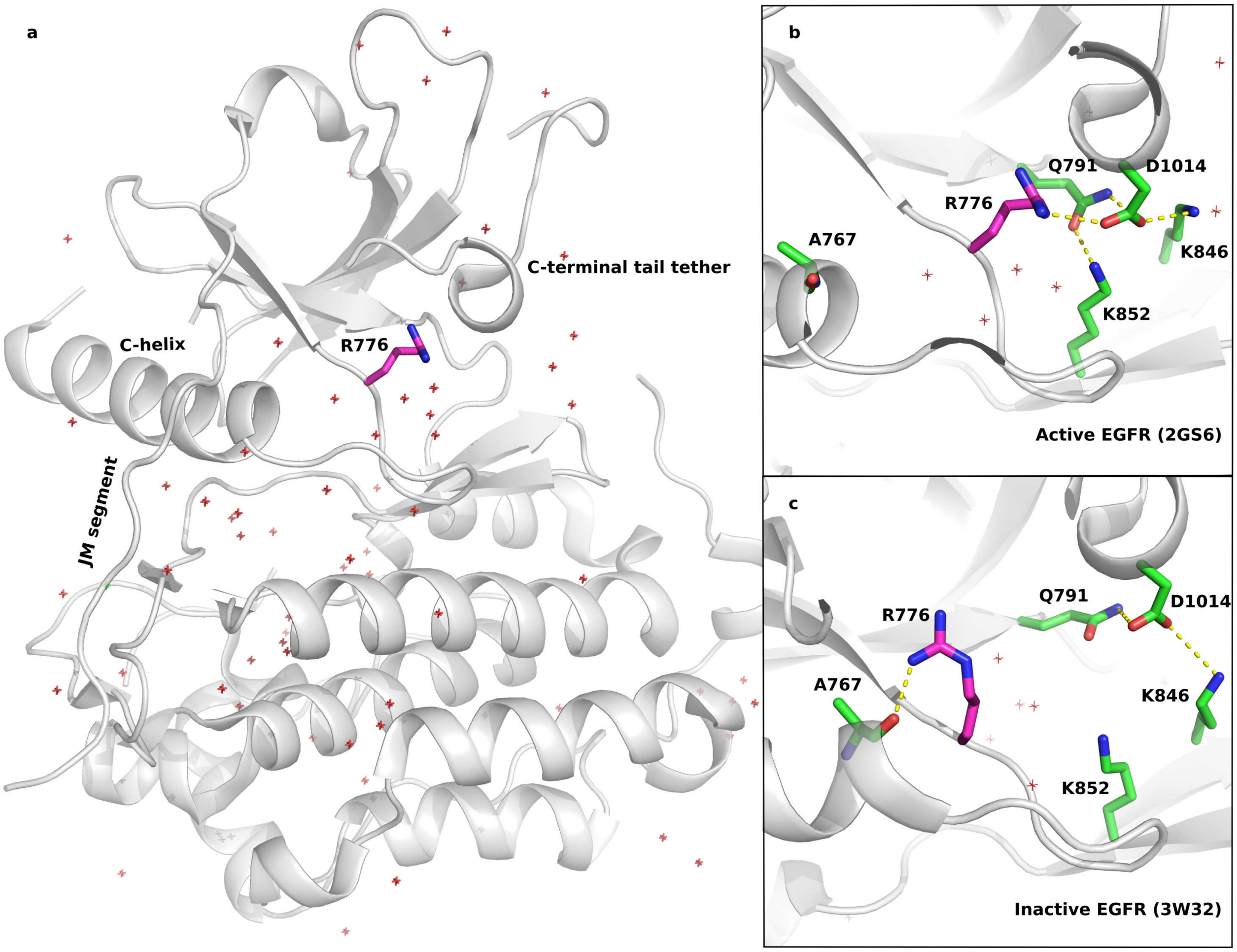


Figure S1: Structure of EGFR showing the position of R776 and associated interactions in active (2GS6) and inactive (3W32) states.

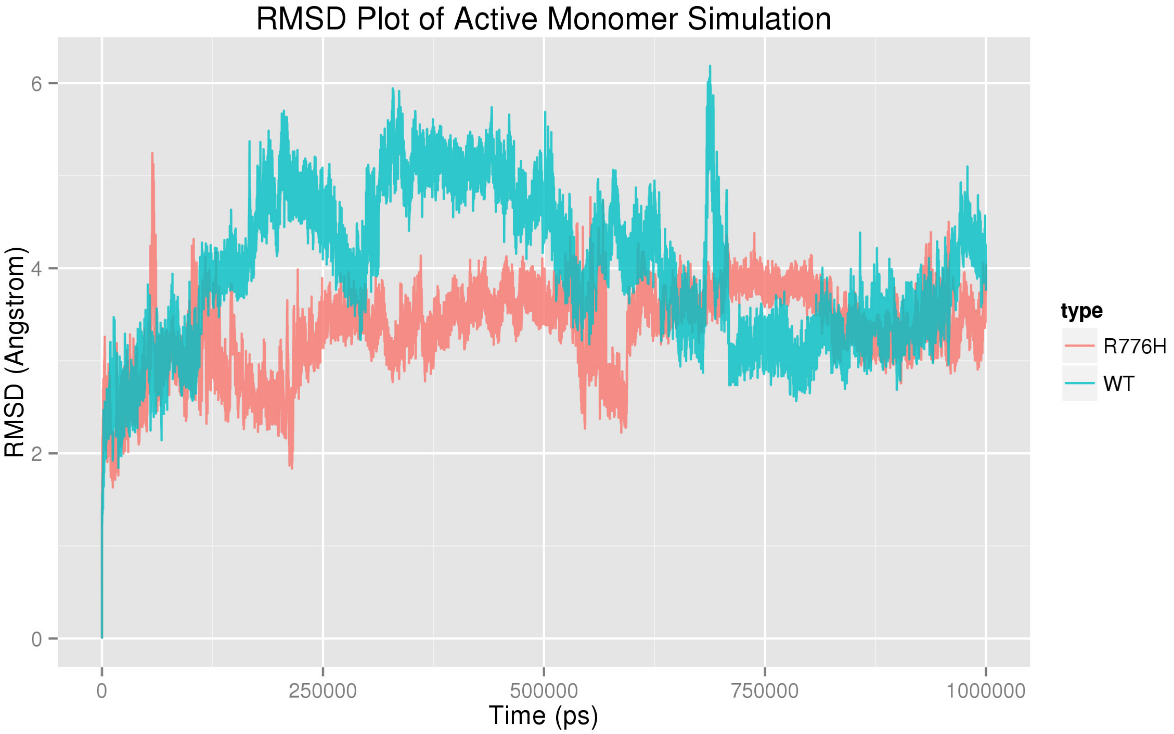


Figure S2: RMSD plot of active monomer simulation of WT (cyan) and R776H (red).

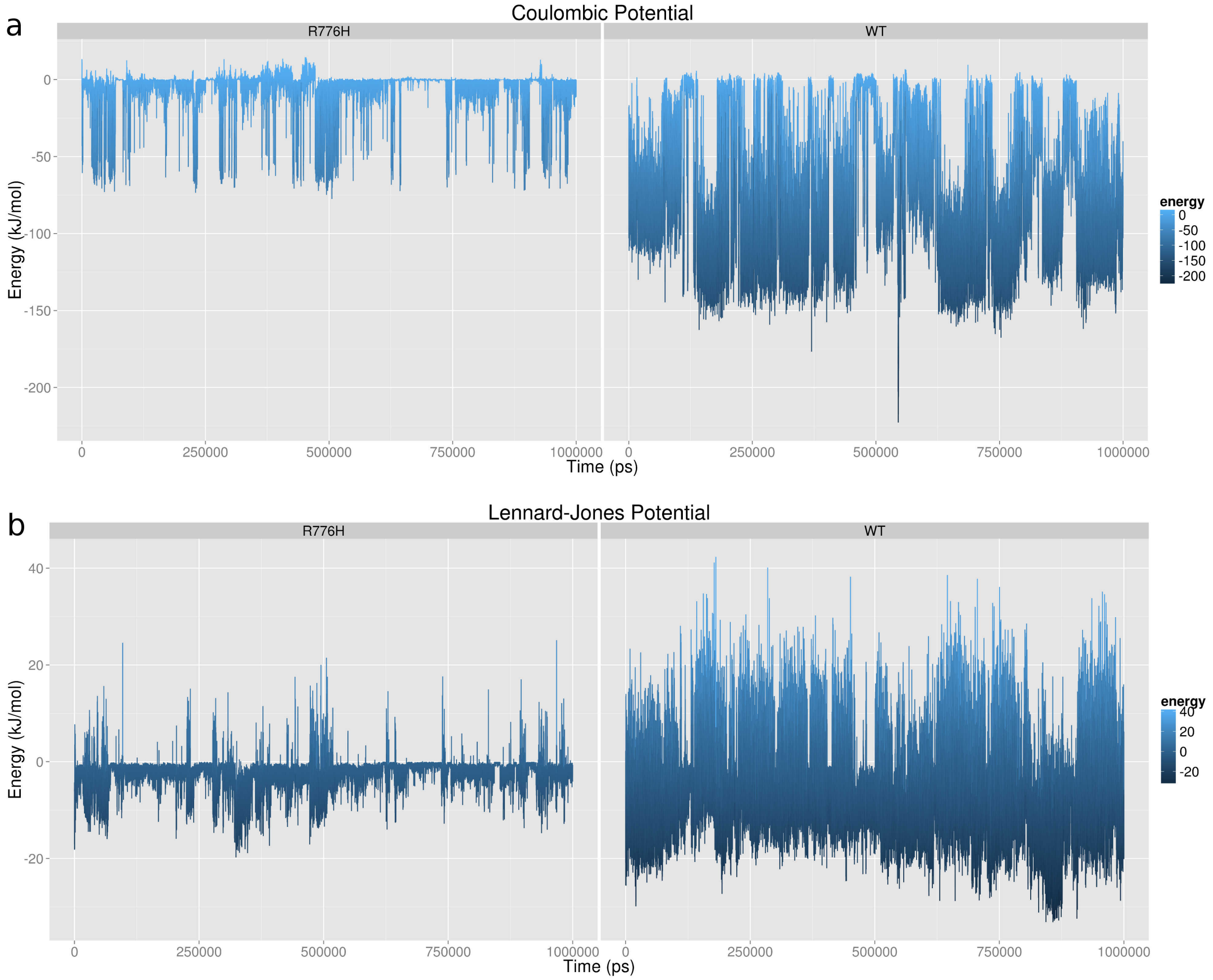


Figure S3: R776H loses the interaction with C-terminal tail of EGFR. a) Coulombic interaction energy profile between R776/H776 and the C-terminal tail tether. b) Van Der Waals interaction energy profile between R776/H776 and the C-terminal tail tether.

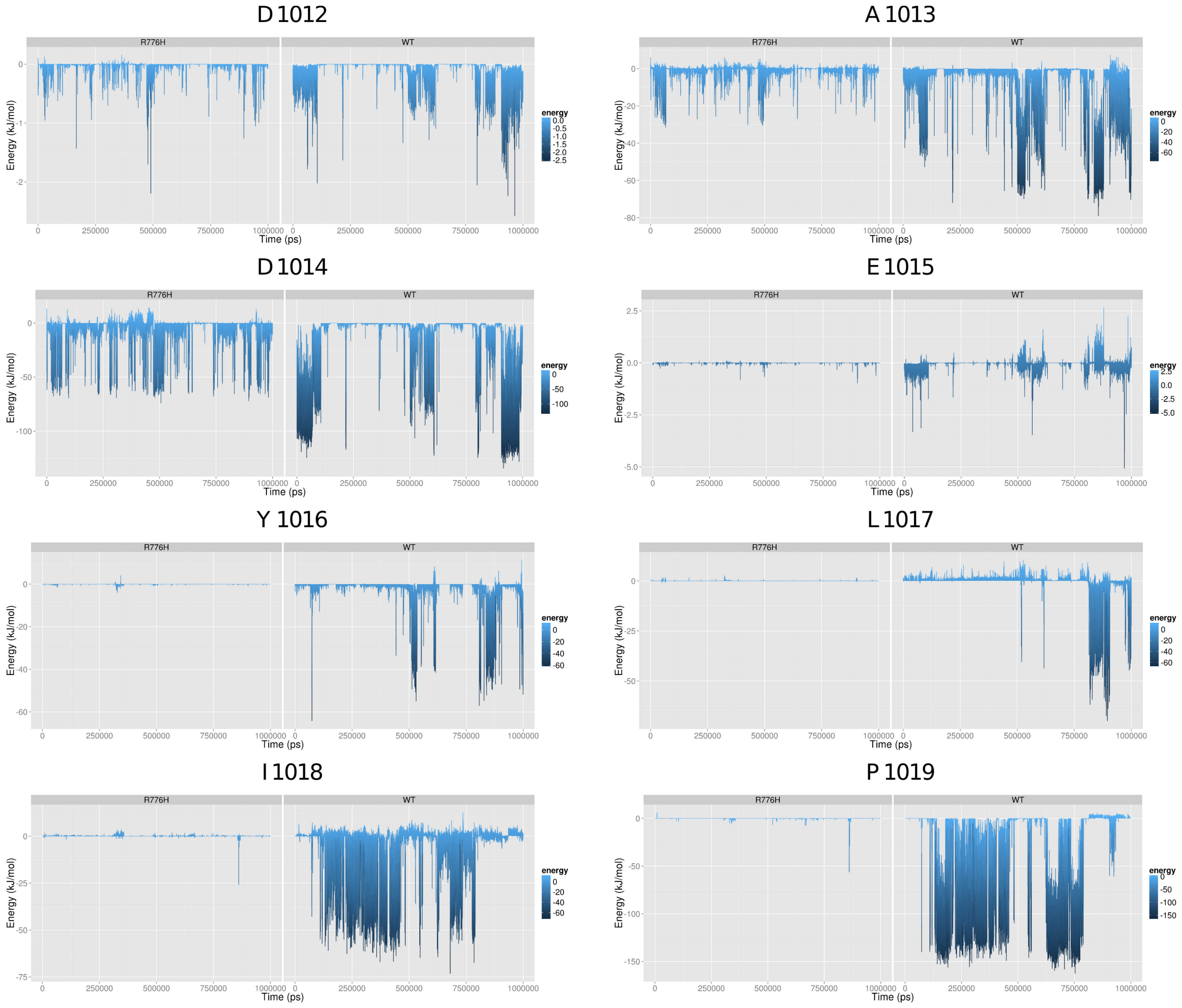
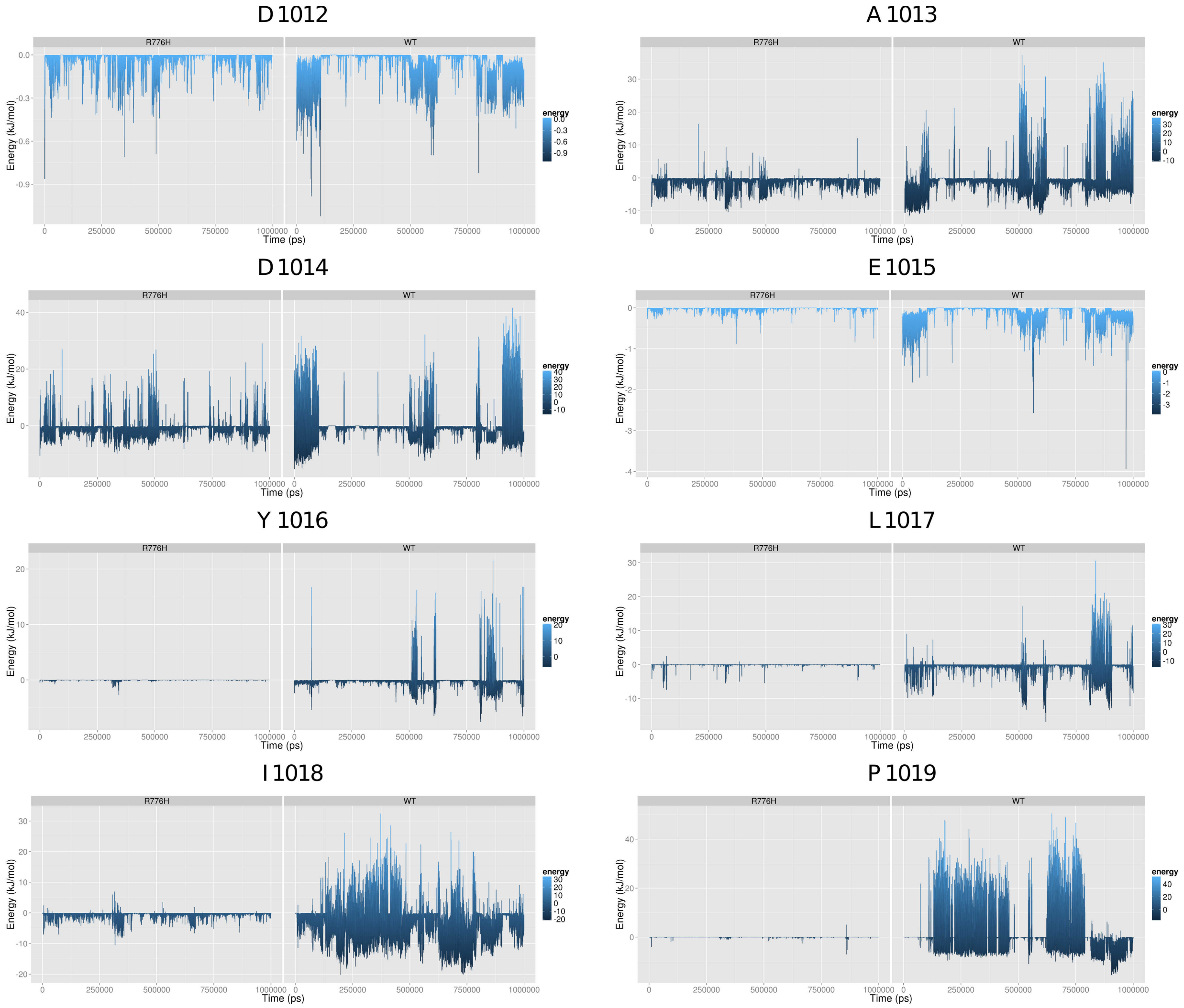


Figure S4: Coulombic interaction between R776/H776 to residues in C-terminal tail tether (D1012, A1013, D1014, E1015, Y1016, L1017, I1018, P1019)


D 1012

A 1013

D 1014

E 1015

Y 1016

L 1017

I 1018

P 1019

Figure S5: Van Der Waals interaction between R776/H776 to residues in C-terminal tail tether (D1012, A1013, D1014, E1015, Y1016, L1017, I1018, P1019)

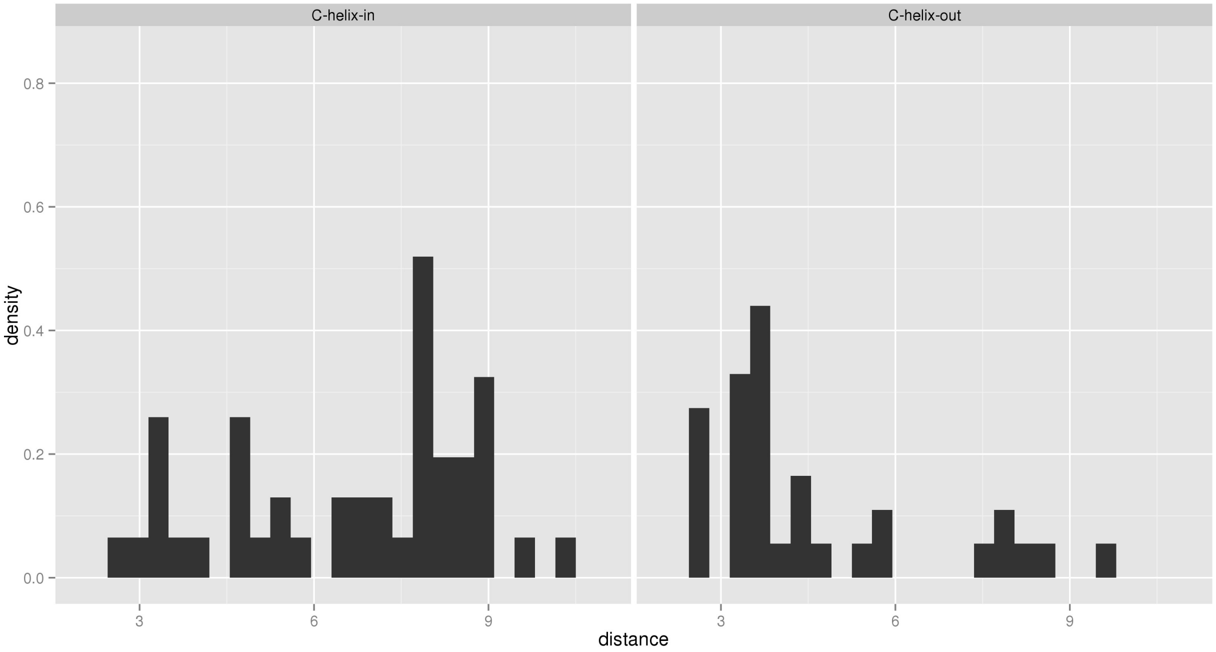


Figure S6: Histogram plot showing the shortest distances between R776(NE,NH1,NH2) to A767(O) between αC-helix "in" crystal structures and αC-helix "out" crystal structures. The list of crystal structures and distances considered in this plot are in Table S1.

Table S1. List of crystal structures considered in Figure S6. αC-helix "in" and "out" are classified manually based on the structural alignment with 2GS6("in") and 1XKK("out").

Table S2. Cancer mutations in the equivalent position of R776 in EGFR of other kinases. Data Source: COSMIC database.