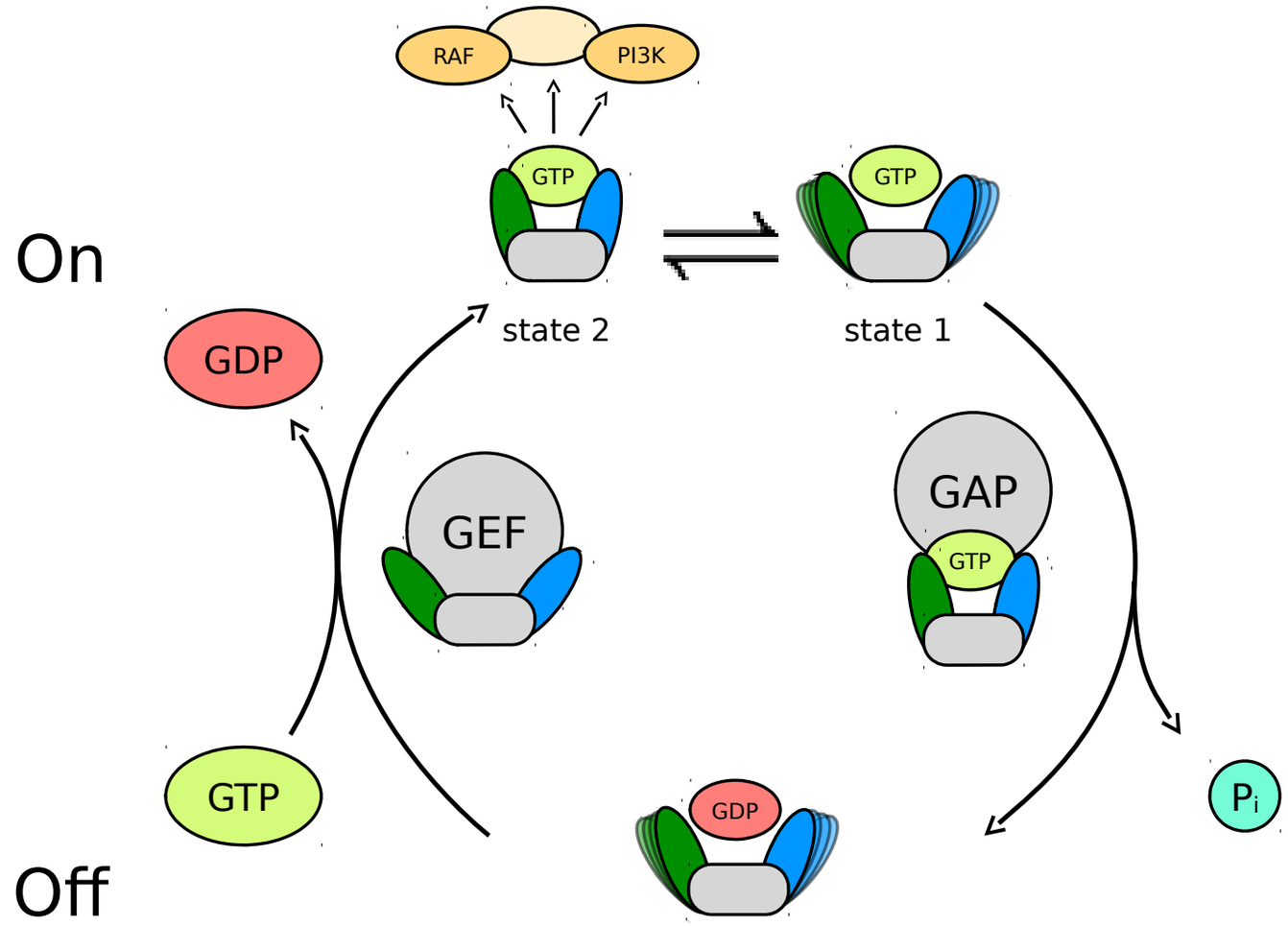
K-Ras: Overview

- GTPase
- Involved in signaling networks for cell differentiation, growth, and division
- Ras family mutations present in 15% of cancers; 85% of those are K-Ras



Two “switch” regions, with two states in the GTP-bound form:
Do oncogenic mutations affect this equilibrium?

K-Ras Q61L: An oncogenic mutation

Q61L

- residue 61 is part of switch 2
- change a charged residue to hydrophobic
- known to be oncogenic (more relevant in H-Ras than K-Ras)

TPS simulations

- multiple state transition path sampling
- separate runs for switch 1 and switch 2 (3 states in each)
- separate runs for wild type and mutant

4 different simulations; only going to look at switch 2 results