

BCH 258 lecture notes Mon. Sept 13, 2010

Roles of the Amino Acids, and mutations to replace them (ref Wrksht3_handedAAroles2009)

• Assignment: WrkSht7-mutations2009:

Graphics: All-atom contacts : (recall howdotswork3KiNG.kin)

• Mutation check: 1lmb6_85aH.kin : in class: show Thr 8 → Val does NOT work!

(WorkSheet homework: show Tyr 22 → Trp does work!)

Thr 8 → Asn NOT work, Asn 58 → Gln NOT work, (Gly 43 → Ser NOT work)

Good N-cap residues, 2 sets: Ser, Thr vs. Asn, Asp

BACKGROUND

Hydrophobic “H” vs Polar “P” : is the most important parameter

“HP” pattern in sequence determines approx. 3D fold, putting most H in, P out

• 1snm.kin, 1snm.omap.gz H in, P out - views of Helix and Loop regions.

“H” : function of Hydrophobic surface area (but Cys also strongly buried)

“P” : function of charge, H-bonding, polarizability (but Pro out, forming corners)

alternating “HP” favors $\uparrow\downarrow\beta$; 3.5 period favors α helix; a run of “P” favors turns;

long run of “H” favors transmembrane; short run of “H” favors $\uparrow\uparrow\beta$

Size, shape, & flexibility of sidechain

Mainchain flexibility: Gly > Ala (and others) > branched C β > Pro > SS

Entropy mutants (native vs unfolded): SS, A → P, G → A

Sidechain degrees of freedom: Hydrophobics ≤ 2 chi's (χ) (except Met 3))

many Polars have more, esp/ Lys & Gln very loose

Aromatics (FYWH): big & flat, help constrain packing

slightly + on edge, - on face,

more often perpendicular than stacked

Pro: not aromatic, not flat; puckers up or down at C γ

ring constrains ϕ near -60° ; good at turns;

good in N-term end of α helix

can do α middle, but bends helix

Ile, Thr sidechains handed: long arm, or Og, on “left” side (arms in front of body)

Sidechains “rotameric”, i.e. few preferred conformations; Ctetr near staggered

Sidechain angles: χ_1, χ_2 , etc. dihedrals (χ_4 max, for Lys & Arg)

for bonds between tetrahedral carbons, staggered >> eclipsed

overall, a few well-defined sidechain conformations are good: rotamers

[only 2 good (4 more OK) for Leu; 13 for Met with 3 χ angles and no branches]



