"nearest neighbor" alignment:

new sequences:

$\}$ N seqs

trusted alignment:

M seqs

1. Find nearest neighbor

2. pairwise alignment to nearest neighbor

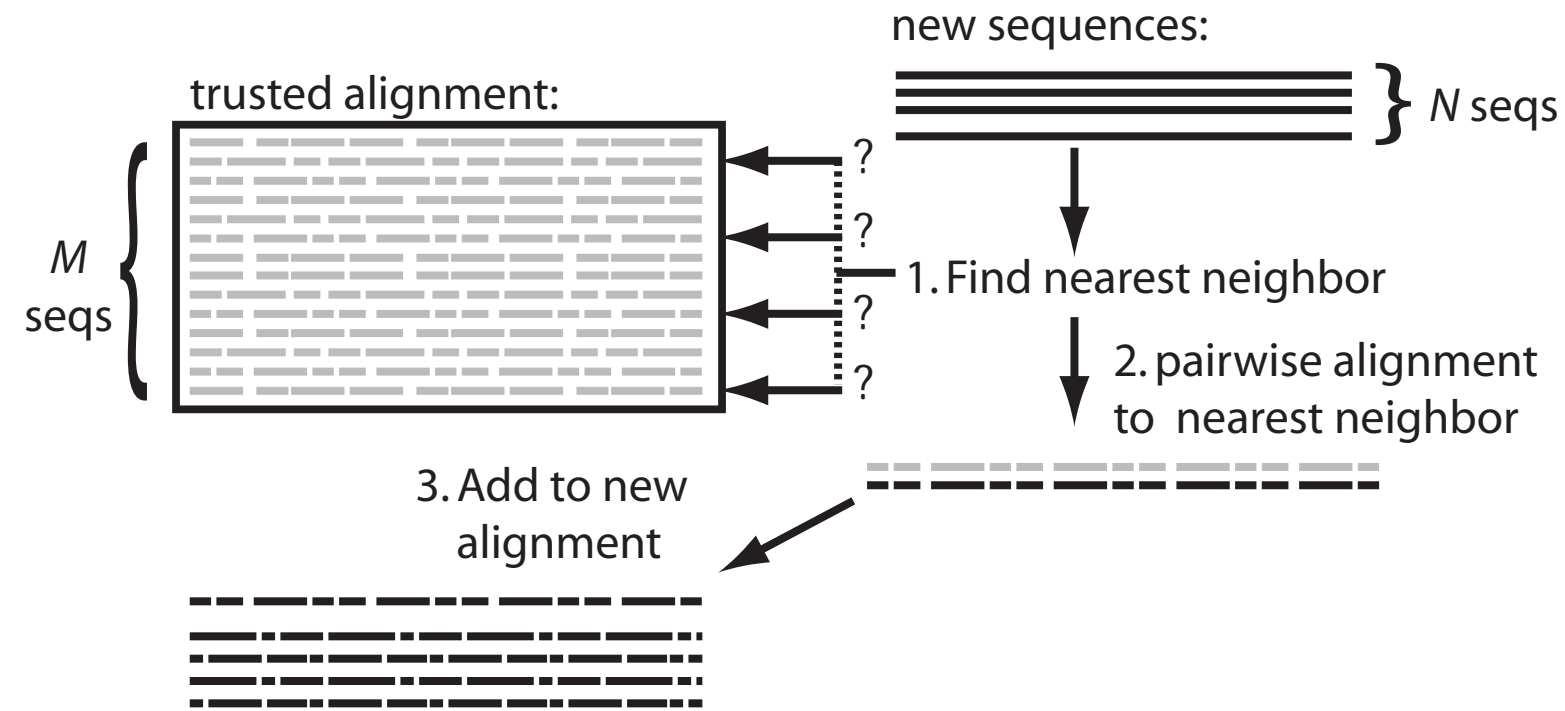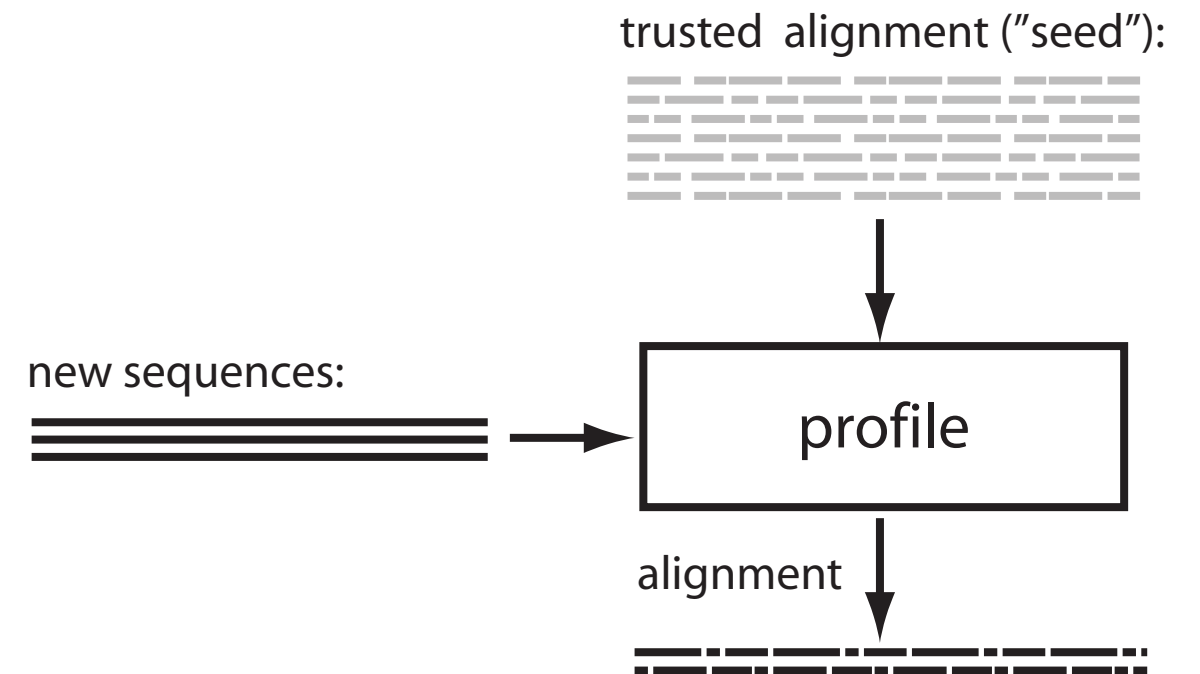3. Add to new alignment

Advantages over *de novo*:
1. More scalable (O(MN))
2. Uses existing, trusted SSU alignment

Drawbacks:
1. Still slow if M is large (~5000 for Greengenes)
2. Pairwise alignment ignores varying conservation across alignment

profile-based alignment:

trusted alignment ("seed"):

new sequences:

profile

alignment

Advantages over *de novo* and nearest-neighbor:
1. Scalable (O(N))
2. Uses existing, trusted SSU alignment
3. Uses position-specific scores

Drawbacks:
1. Only *consensus* positions are aligned, other nucleotides are *inserted*
2. Ignorant of phylogeny