ACGGATTAGAT-Sequence: Construct seed matches GCCGTACG CCCCCTTT GCCGTACG CCCCCTTT GCCGTACG CCCCCTTT Chain seed matches within w nucleotides of each other Chained seeds and flanking sequence: AAAAAAAATGGGAAGCCGTACGTCCCCCTTTGCATAACTACGACTA TTGGCGGGGTGGGAAGCCGTACGCCCCCCTTTGCATAAGTAGGTCTT GCAATACCCTGGGAAGCCGTACGAACCCCCTTTGCATAAGGTCTTACT Align regions between seeds AAAAAAAAATGGGAAGCCGTACGT-CCCCCTTTGCATAACTACGACTA TTGGCGGGGTGGGAAGCCGTACGC-CCCCCTTTGCATAACTAGGTCTT GCAATACCCTGGGAAGCCGTACGAACCCCCTTTGCATAAGGTCTTACT Align regions flanking the chain AAAAAAAATGGGAAGCCGTACGT-CCCCCTTTGCATAACTACGACTA---TTGGCGGGG-----TGGGAAGCCGTACGC-CCCCCTTTGCATAACTAGGTCTT------AATACCCTGGGAAGCCGTACGAACCCCCTTTGCATAA---GGTCTTACT Detect unrelated regions with Posterior probabilty of unrelated sequence: a hidden Markov model 1 vs 2 2 vs 3 1 vs 3 0.5 Apply transitive homology (change to 1 vs 3) Unalign non-homologous regions and trim alignment boundaries TGGGAAGCCGTACGT-CCCCCTTTGCATAACTACGACTA Final local multiple TGGGAA<mark>GCCGTACG</mark>C-CCCCCTTTGCATAACTAGGTCTT alignment: TGGGAA<mark>GCCGTACG</mark>AACCCCCTTTGCATAA---GGTCTT