Consider the directed acyclic graph G=(V,E) constructed in class, with vertices s in the upper left corner and t in the lower right corner, whose s-t paths correspond to global alignments between A and B. For a set of edges  $F \subset E$ , let c(F) denote the total cost of the edges in F. If P is a path in G, let  $\Delta(P)$  denote the set of diagonal edges in P (i.e. the matches in the alignment).

Let Q denote the s-t path corresponding to the given alignment. Let  $E_1$  denote the horizontal or vertical edges in G (corresponding to indels),  $E_2$  denote the diagonal edges in G that do not belong to  $\Delta(Q)$ , and  $E_3 = \Delta(Q)$ . Note that  $E = E_1 \cup E_2 \cup E_3$ .

Let  $\varepsilon = 1/2n$  and  $\varepsilon' = 1/4n^2$ . We form a graph G' by subtracting  $\varepsilon$  from the cost of every edge in  $E_2$  and adding  $\varepsilon'$  to the cost of every edge in  $E_3$ . Thus, G' has the same structure as G, but a new cost function c'.

Now we claim that path Q is a minimum-cost s-t path in G' if and only if it is the unique minimum-cost s-t path in G. To prove this, we first observe that

$$c'(Q) = c(Q) + \varepsilon'|\Delta(Q)| \le c(Q) + \frac{1}{4},$$

and if  $P \neq Q$ , then

$$c'(P) = c(P) + \varepsilon'|\Delta(P \cap Q)| - \varepsilon|\Delta(P - Q)| \ge c(P) - \frac{1}{2}.$$

Now, if Q was the unique minimum-cost path in G, then  $c(Q) \leq c(P) + 1$  for every other path P, so c'(Q) < c'(P) by the above inequalities, and hence Q is a minimum-cost s-t path in G'. To prove the converse, we observe from the above inequalities that c'(Q) - c(Q) > c'(P) - c(P) for every other path P; thus, if Q is a minimum-cost path in G', it is the unique minimum-cost path in G.

Thus, the algorithm is to find the minimum cost of an s-t path in G', in O(mn) time and O(m+n) space by the algorithm from class. Q is the unique minimum-cost A-B alignment if and only if this cost matches c'(Q).

 $<sup>^{1}</sup>$ ex485.507.165