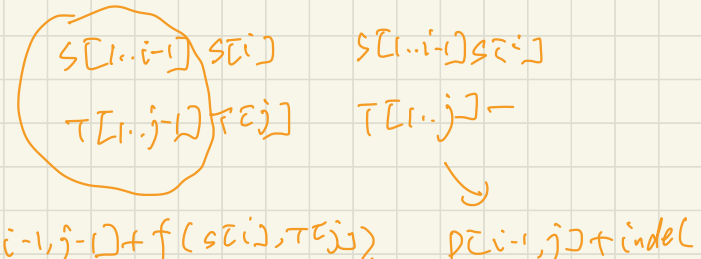
Review:

- Alignment for bio-sequence comparison
- Dynamic programming algorithm
  - define subproblems: $D[i,j]$ = optimal align score of $S[1..i]$, $T[1..j]$
  - recurrence relation
  - base case
  - order of computation
  - back tracking.
- practical tricks
  - linear space score
  - compute the "pointers" during backtracking
- gap penalty
  - arbitrary $g(k)$



Affine gap penalty example

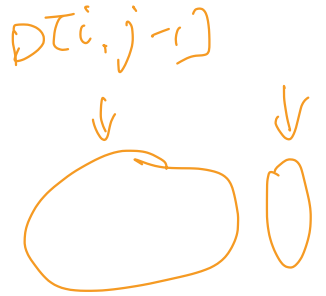
For example: match = 1; mismatch = -1; gap open = -5; gap extension = -1.

- ATAGG--AAG
- || || | |
- ATTGGCAATG
- 6 match, 2 mismatch, 1 gap open, 2 gap extension, score = ?
- ATAGG-AA-G
- || || || |
- ATTGGCAATG

6-2 -5-2 = -3

7-1 -5-1 -5-1 = -6.

Old Algorithm Does not Work

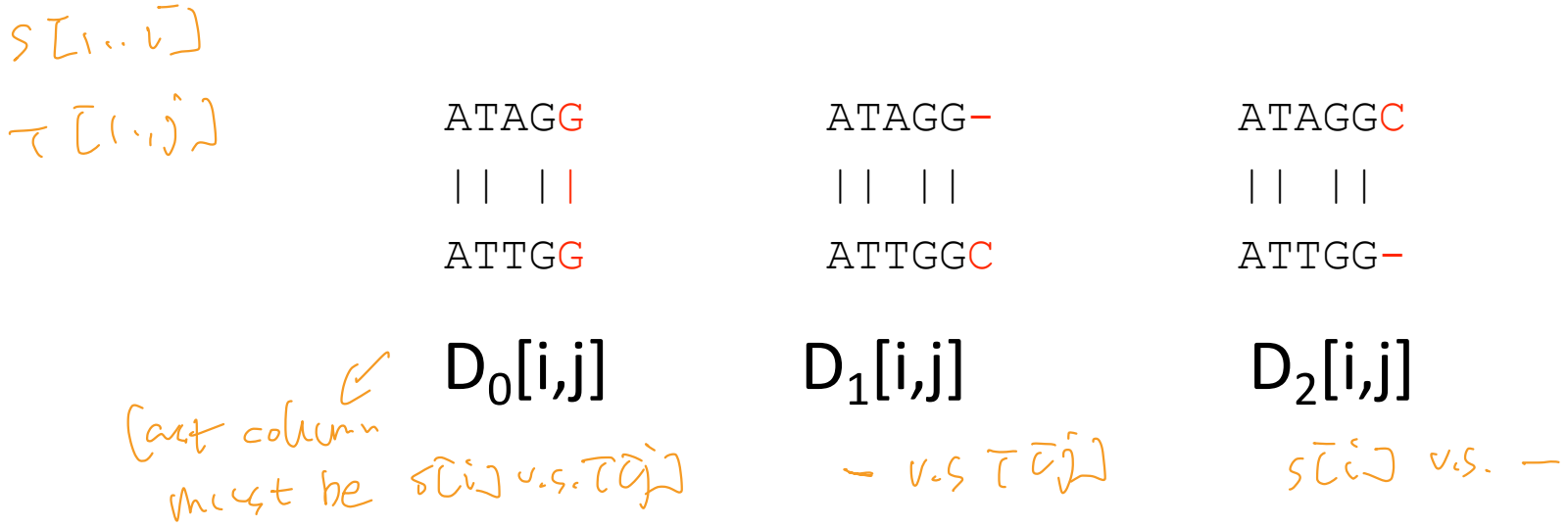


- Consider the last column of an alignment again:

- When the last column is an indel, the added cost depends on the previous column.
  - If previous column has a gap opened already, then
  - D[4,6] = D[4,5] + gapext
  - Else
  - D[4,6] = D[4,5] + gapopen + gapext
- How do we know the previous column's configuration?
- Because by induction we know the optimal solution for D[i,j-1], can we simple look at it and use the configuration?

Algorithm for Affine Gap

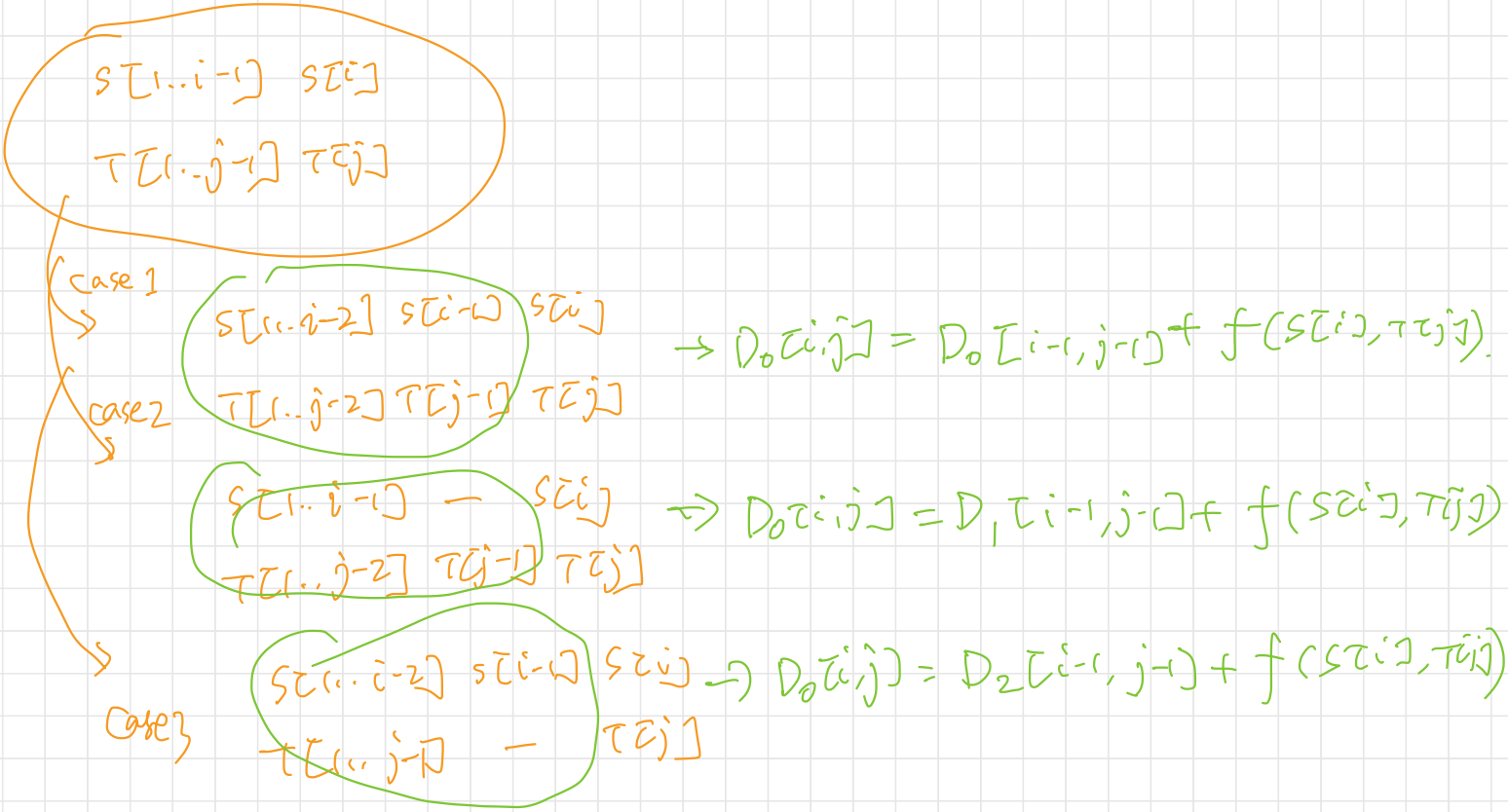
- We compute the optimal solution by limiting the last column to one of the following three configurations:



- We only distinguish them by the last column, there is no constraint for columns before the last column.

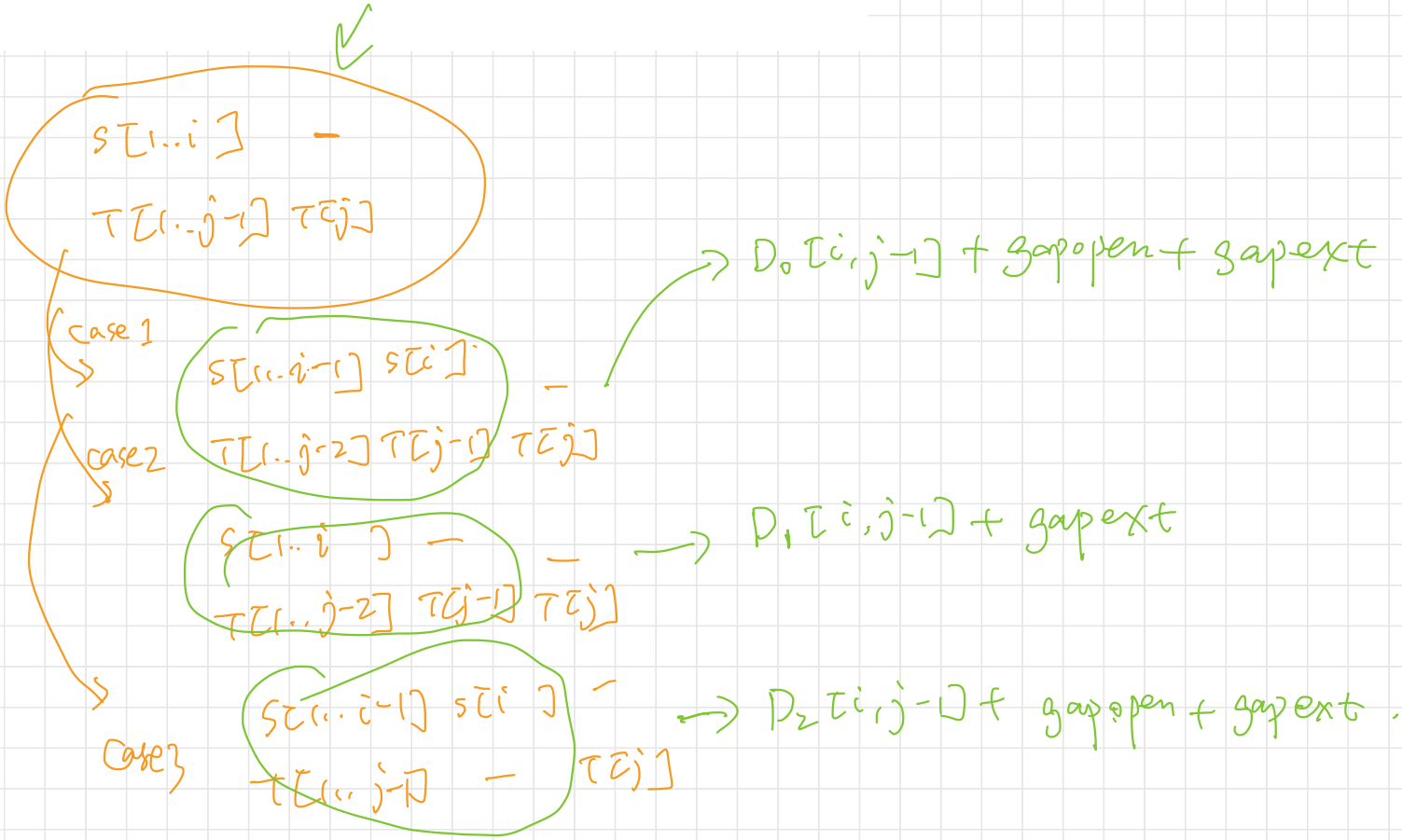
```
ATAGG      ATAGG-     ATAGGC
|| ||      || ||      || ||
ATTGG      ATTGGC     ATTGG-
```

$D_0[i,j]$ $D_1[i,j]$ $D_2[i,j]$



```
ATAGG      ATAGG-     ATAGGC
|| ||      || ||      || ||
ATTGG      ATTGGC     ATTGG-
```

$D_0[i,j]$ $D_1[i,j]$ $D_2[i,j]$



Recurrence Relation

$$D_0[i,j] = f(s[i], t[j]) + \max \begin{cases} D_0[i-1, j-1]; \\ D_1[i-1, j-1]; \\ D_2[i-1, j-1]; \end{cases}$$

$$D_1[i,j] = gapext + \max \begin{cases} D_0[i, j-1] + gapopen; \\ D_1[i, j-1]; \\ D_2[i, j-1] + gapopen; \end{cases}$$

$$D_2[i,j] = gapext + \max \begin{cases} D_0[i-1, j] + gapopen; \\ D_1[i-1, j] + gapopen; \\ D_2[i-1, j]; \end{cases}$$

Note the grayed cases can't be optimal so can be safely removed.

Algorithm

- No difference to the simple DP but now uses three arrays.
- Backtracking should be very careful!
- Still O(nm) time. Approximately 3 times slower.
- This is okay because the model is more expressive.
- Much faster than the general gap penalty.

Gotoh, O., 1982. An improved algorithm for matching biological sequences. *Journal of molecular biology*, *162*(3), pp.705-708.