14 February 2024. RNA Folding

Plan.

* RNA Folding Problem

* Announcements

* A different flavor of DP.

Another problem from biology

<u>RNA Sequences</u> $m \in \{A, U, C, G\}^*$

$m = A\,U\,U\,C\,G\,G\,A\,C\,G\,G\,A\,A$

<u>Key Question</u>:

What <u>structure</u> does the RNA molecule adopt?

What structure does the RNA molecule adopt?

↳ Base pairing

A — U

C — G

$$BP = \{(A,U), (U,A), (C,G), (G,C)\}$$

What structure does the RNA molecule adopt?

m = A U U C G G A C G G A A

$\downarrow$ base pairing

What structure does the RNA molecule adopt?

m = A U U C G G A C G G A A

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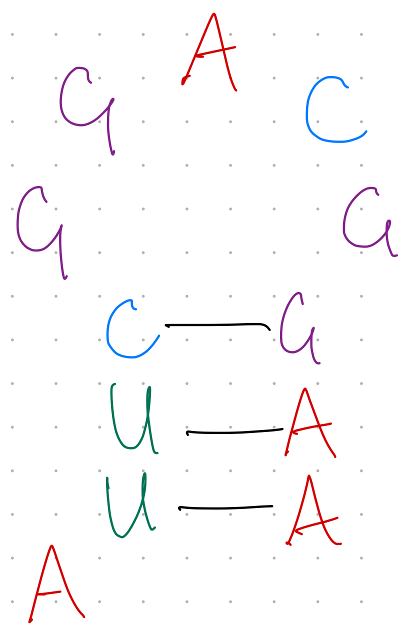


<u>Given</u>: RNA Sequence $m \in \{A, U, C, G\}^*$

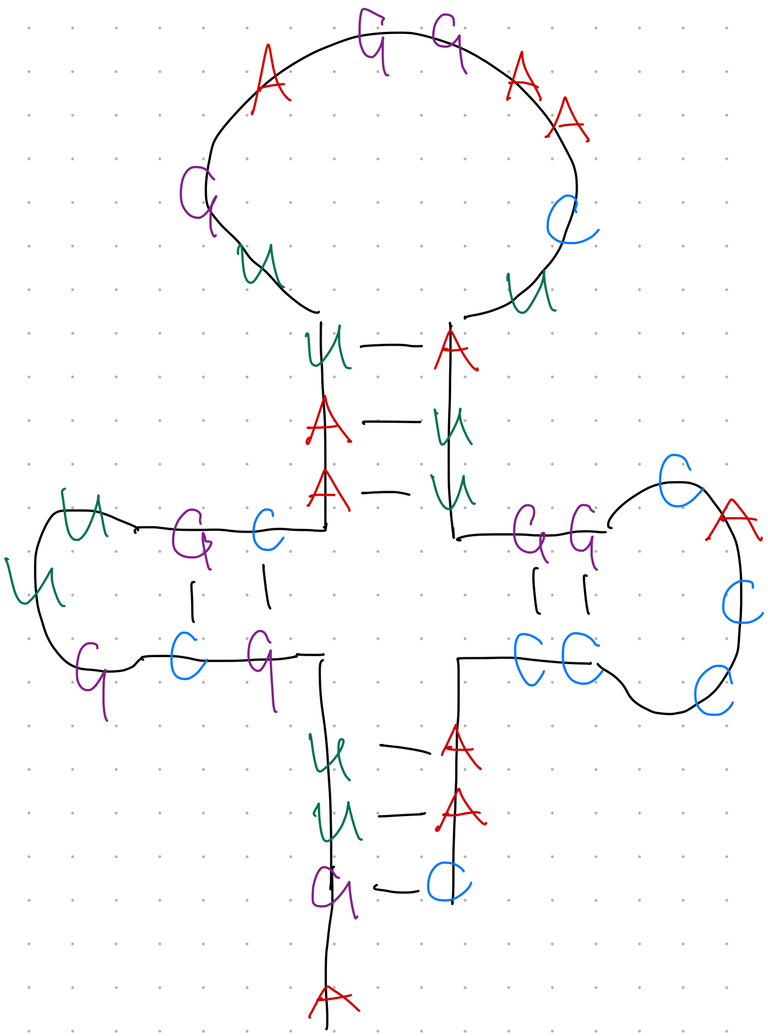
<u>Find</u>: Minimum "energy" structure

A G U U G C G U U G C A A U U G A G G A A C U A U U G G C A C C C C A A C

Given: RNA sequence $m \in \{A, U, C, G\}^*$

Find: Minimum "energy" structure

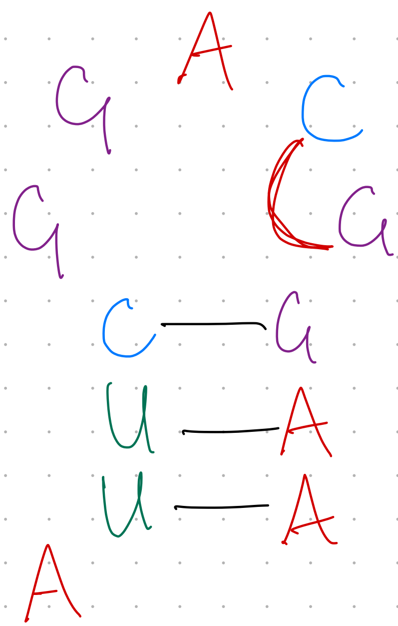
AGUUGCGUUGCAAUUGAGGAACUAUUGGCACCCCAAC



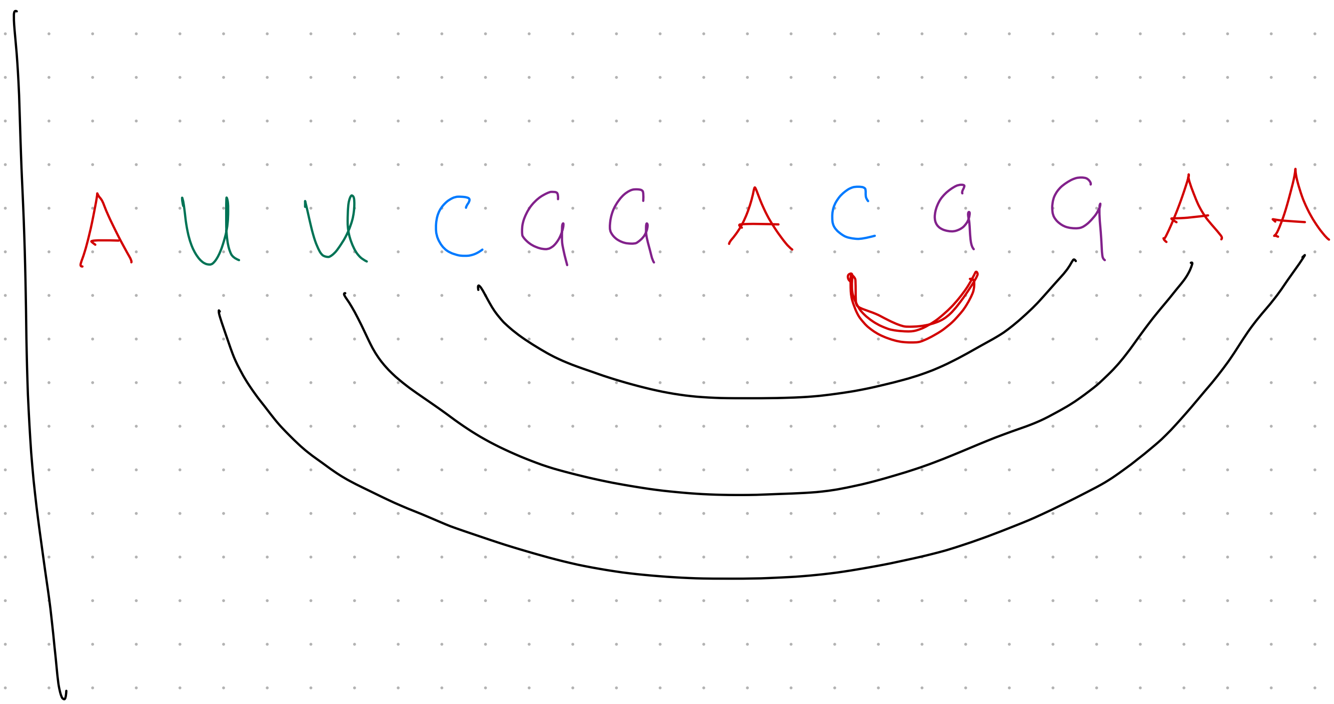
Min "energy" $\equiv$ Max "legal" base pairing

Given: RNA sequence $m \in \{A, U, C, G\}^*$

Compute: Maximum Non-crossing matching E of preferred base pairs within m.



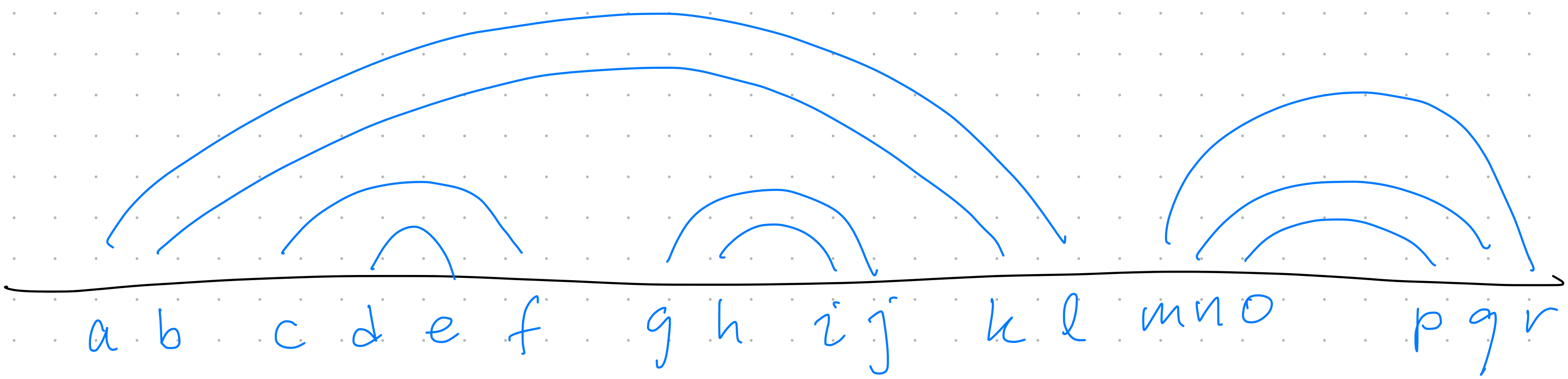
$\Rightarrow$



Given: RNA sequence $m \in \{A, U, C, G\}^*$

Compute: Maximum Non-crossing matching E of preferred base pairs within m.

$m =$



$$E = \{ (a,l), (b,k), (c,f), (d,e), \ldots \quad (m,r), (n,q), (o,p) \}$$

<u>Given</u>: RNA sequence $m \in \{A, U, C, G\}^*$

<u>Compute</u>: Maximum <u>Non-crossing</u> matching E of preferred base pairs within m.

<u>Non-crossing</u>: if $(i, j), (k, \ell) \in E$

then, $\neg (i < k < j < \ell)$.

$m_i \cdots m_k \cdots m_j \cdots m_\ell$

Announcements

* HW1 Grades Released
* HW3 Due Tomorrow 11:59pm
* Prelim Next Week

  Feb 20, 7:30 pm

  Uris G01, Olin 155, Olin 165

  See Ed for room assignment

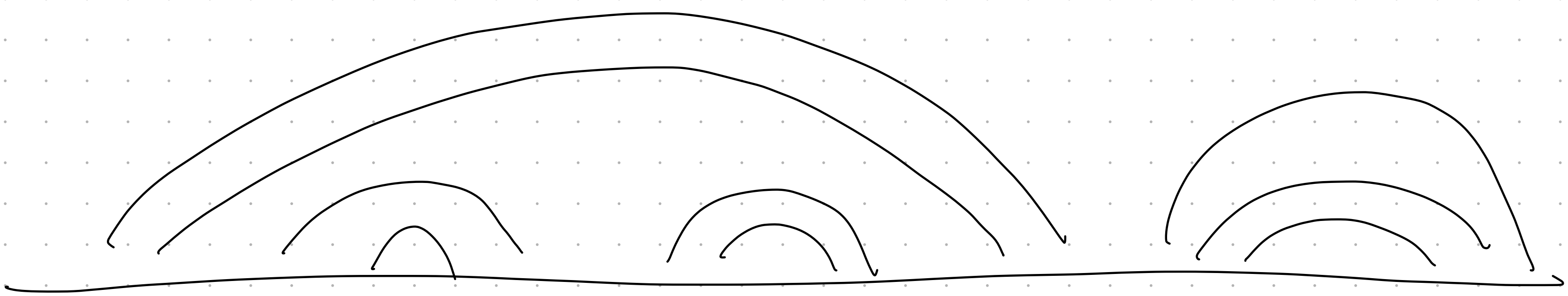
* Prelim Reviews: Gates G01

  Saturday 1-3:30 pm

  Sunday 2-4:30 pm

Dynamic Programming Approach

* Express Complete Solution in terms of subsolutions

$m =$ 

Dynamic Programming Approach

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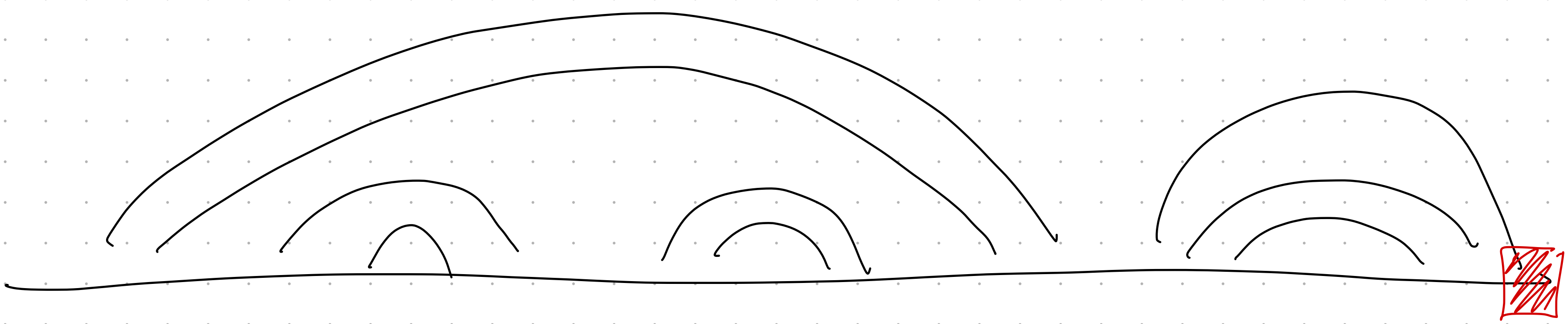
$m =$ 

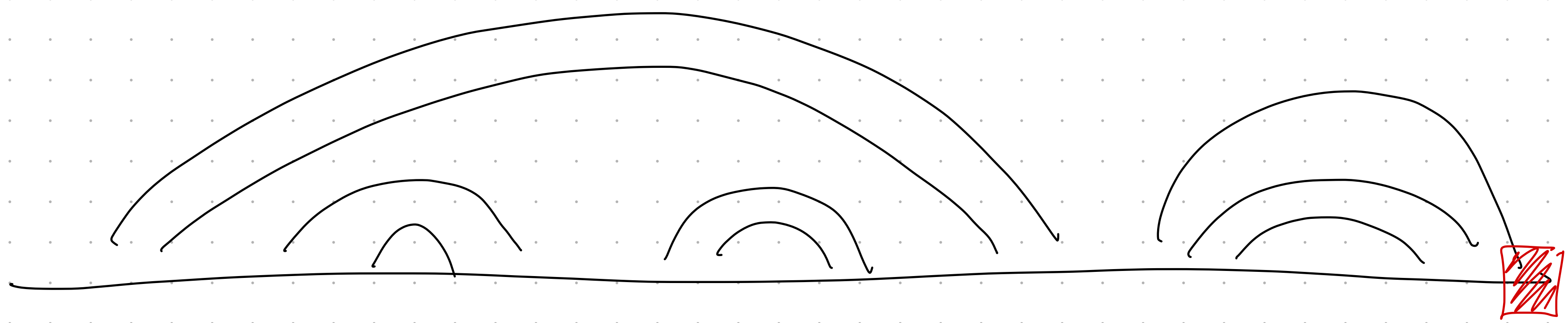
$m_n \in E$

OR

$m_n \notin E$

Dynamic Programming Approach

* Express Complete Solution in terms of subsolutions

$m =$ 

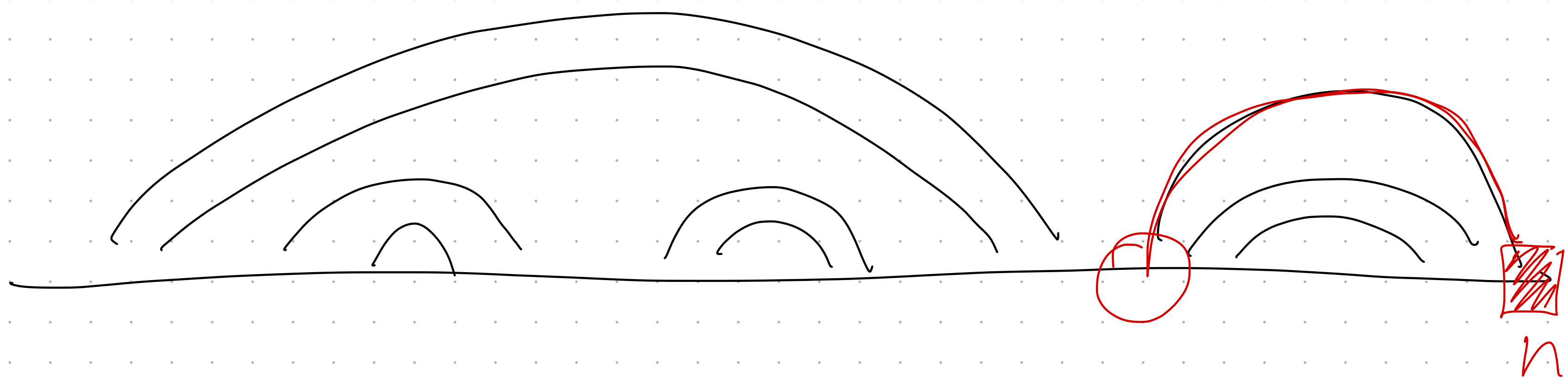
$m_n \in E$

OR

$OPT[n] = OPT[n-1] \longleftarrow m_n \notin E$

Dynamic Programming Approach

* Express Complete Solution in terms of subsolutions

$m =$ 

$m_n \in E$

Dynamic Programming Approach

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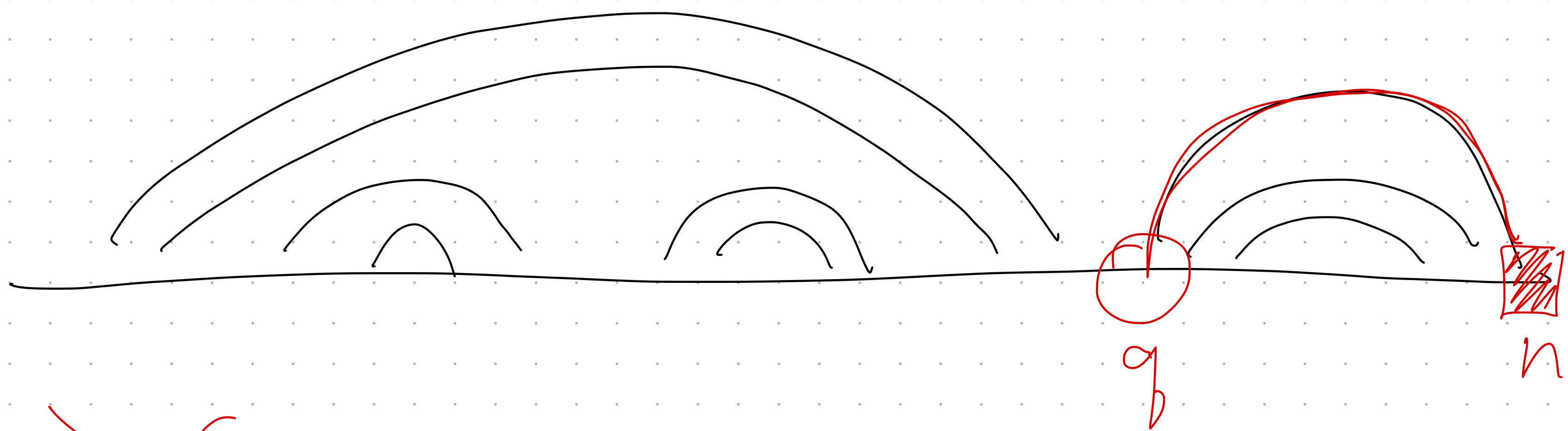
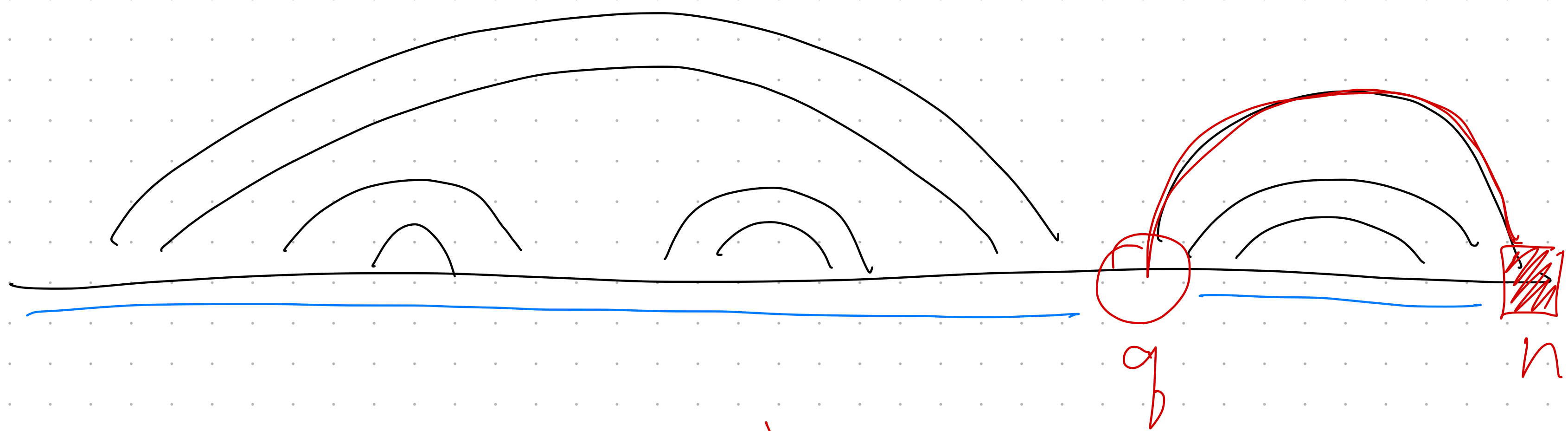
$m =$ 

$\cancel{m_n \in E}$

$\exists\, q \in [n]$ s.t. $(m_q, m_n) \in E$

Dynamic Programming Approach

* Express Complete Solution in terms of subsolutions

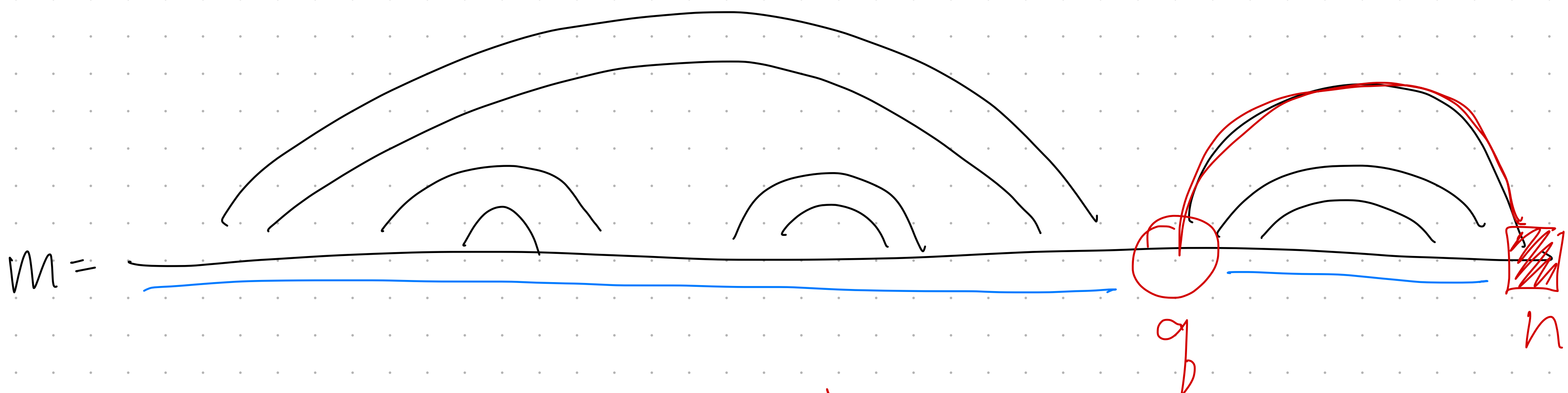
$m =$ 

$\exists q \in [n]$ s.t. $(m_q, m_n) \in E$

What are the subproblems?

Dynamic Programming Approach

* Express Complete Solution in terms of subsolutions



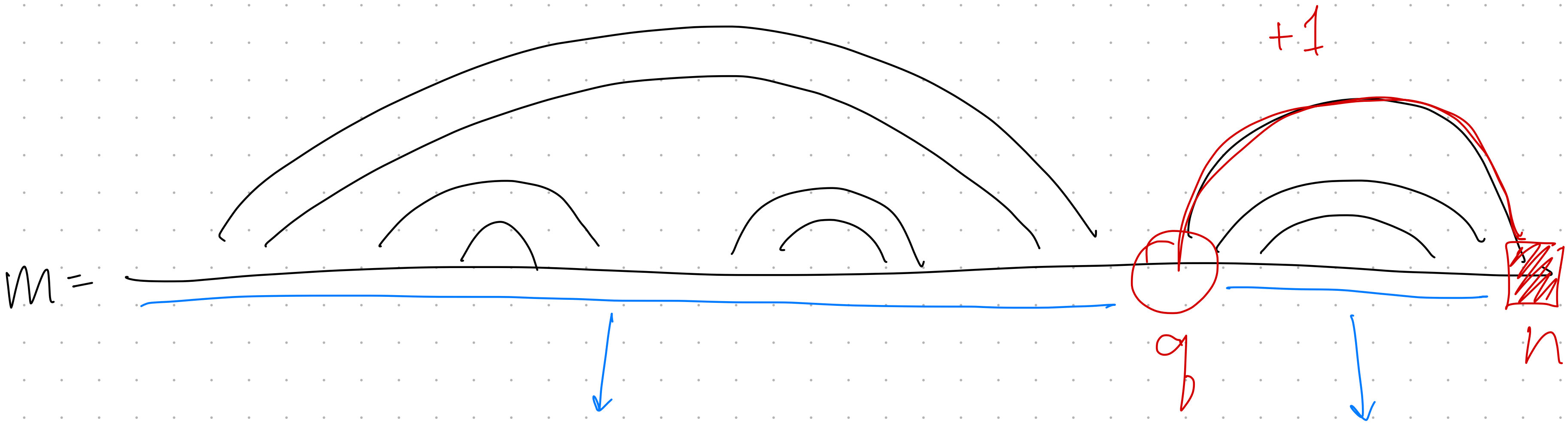
$\exists\, q \in [n]$ s.t. $(m_q, m_n) \in E$

$$OPT[n] = OPT[q-1] + \underline{\quad ?? \quad}$$

Solution: 2D Dynamic Programming Table

(even though "1D" problem)

$OPT[p, r]$ = Best non-crossing match on substring from $p \rightarrow r$



$OPT[1, q-1] \quad + \quad OPT[q+1, n-1]$

Solution 2D Dynamic Programming Table

(even though "1D" problem)

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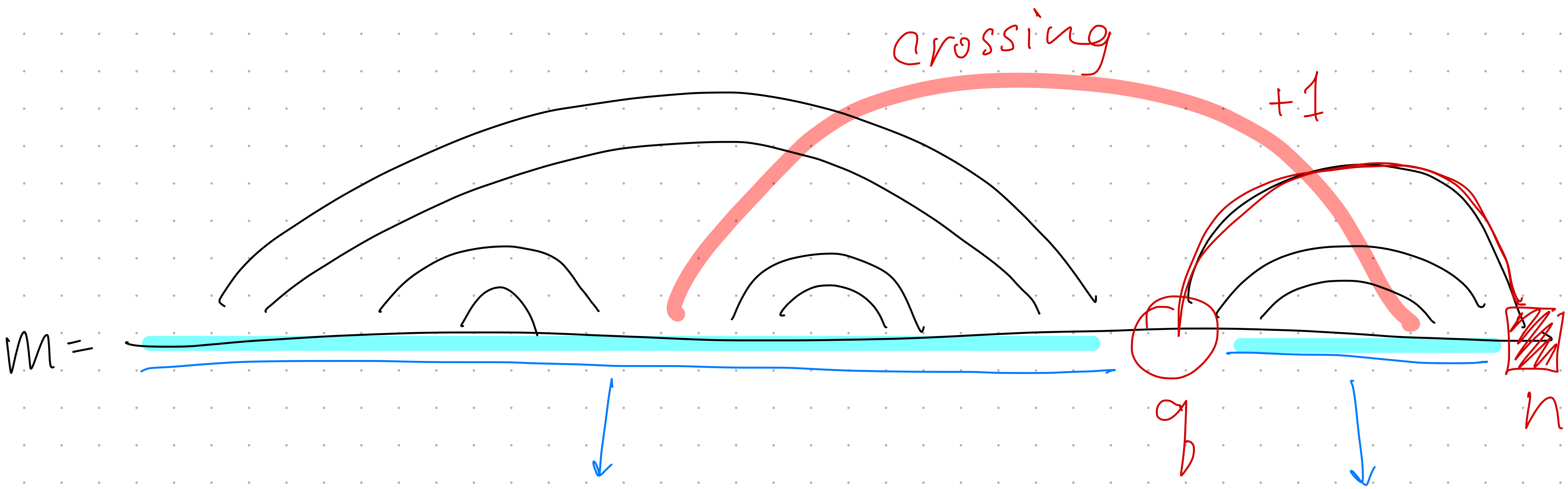

$OPT[1, q-1] \quad + \quad OPT[q+1, n-1]$

DP Recurrence: Fix $p < r$.

$OPT[p, r] =$

① M_r not involved

$OPT[p, r-1]$

② M_r involved

$\Rightarrow$ Find best legal q

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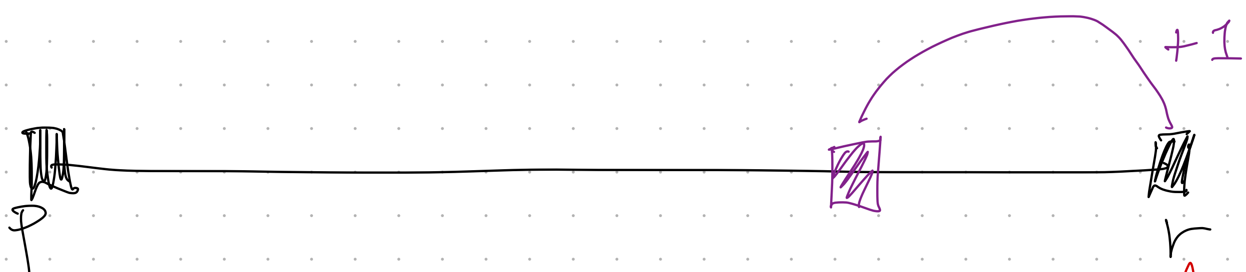


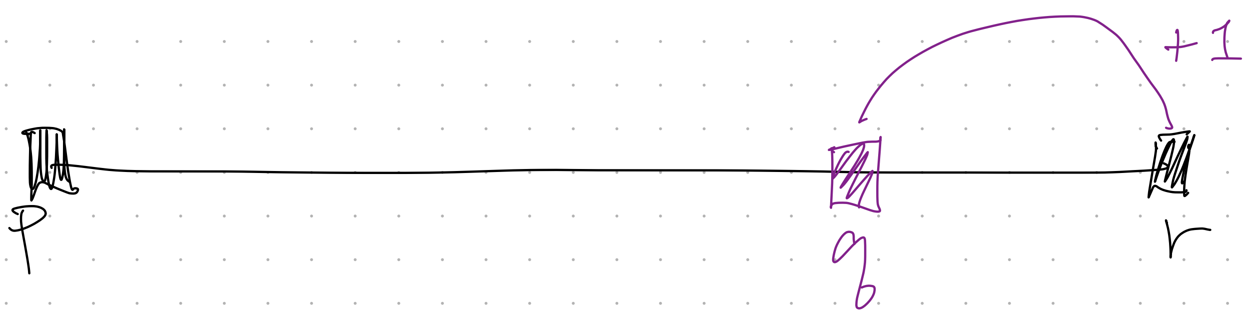
$$BP = \left\{ \begin{array}{ccc} U & — & A \\ A & — & U \\ G & — & C \\ C & — & G \end{array} \right\}$$

DP Recurrence. Fix $p < r$.

① M_r not involved
$OPT[p, r-1]$

$OPT[p, r] =$

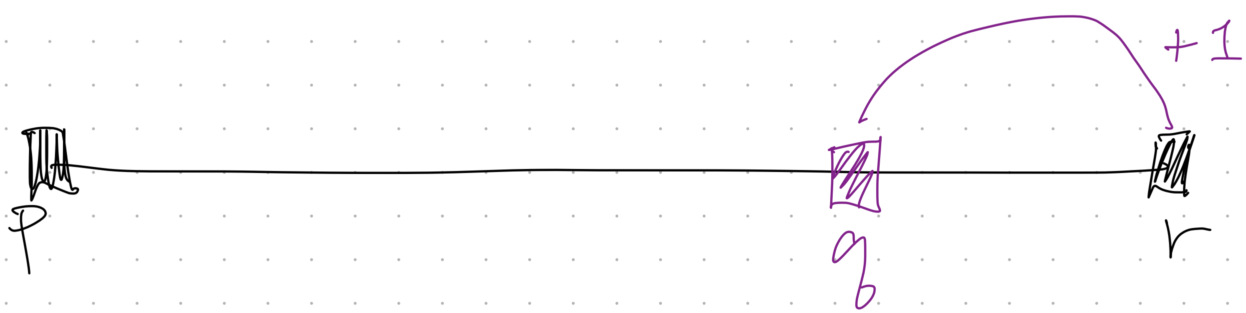
② M_r involved
$\Rightarrow$ Find <u>best</u> legal q



$$\max_{\substack{q \in [p+1, r-1] \\ \text{s.t. } (M_q, M_r) \in BP}} \left\{ 1 + OPT[p, q-1] + OPT[q+1, r-1] \right\}$$

DP Recurrence. Fix $p < r$.

$$\mathrm{OPT}[p, r] = \begin{cases} \text{① } M_r \text{ not involved:} & \mathrm{OPT}[p, r-1] \\ \text{② } M_r \text{ involved} \implies \text{Find } \underline{\text{best}} \text{ legal } q & \end{cases}$$



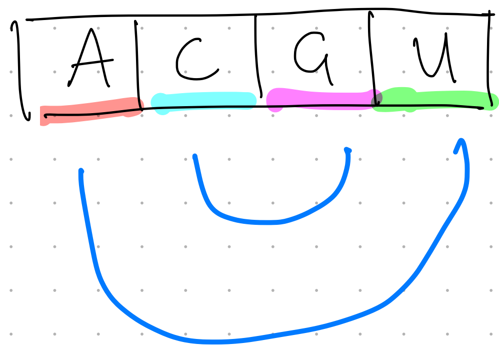
$$\max_{\substack{q \in [p+1, r-1] \\ \text{s.t. } (M_q, M_r) \in BP}} \left\{ 1 + \mathrm{OPT}[p, q-1] + \underbrace{\mathrm{OPT}[q+1, r-1]}_{\text{edge cases?}} \right\}$$

DP Recurrence.

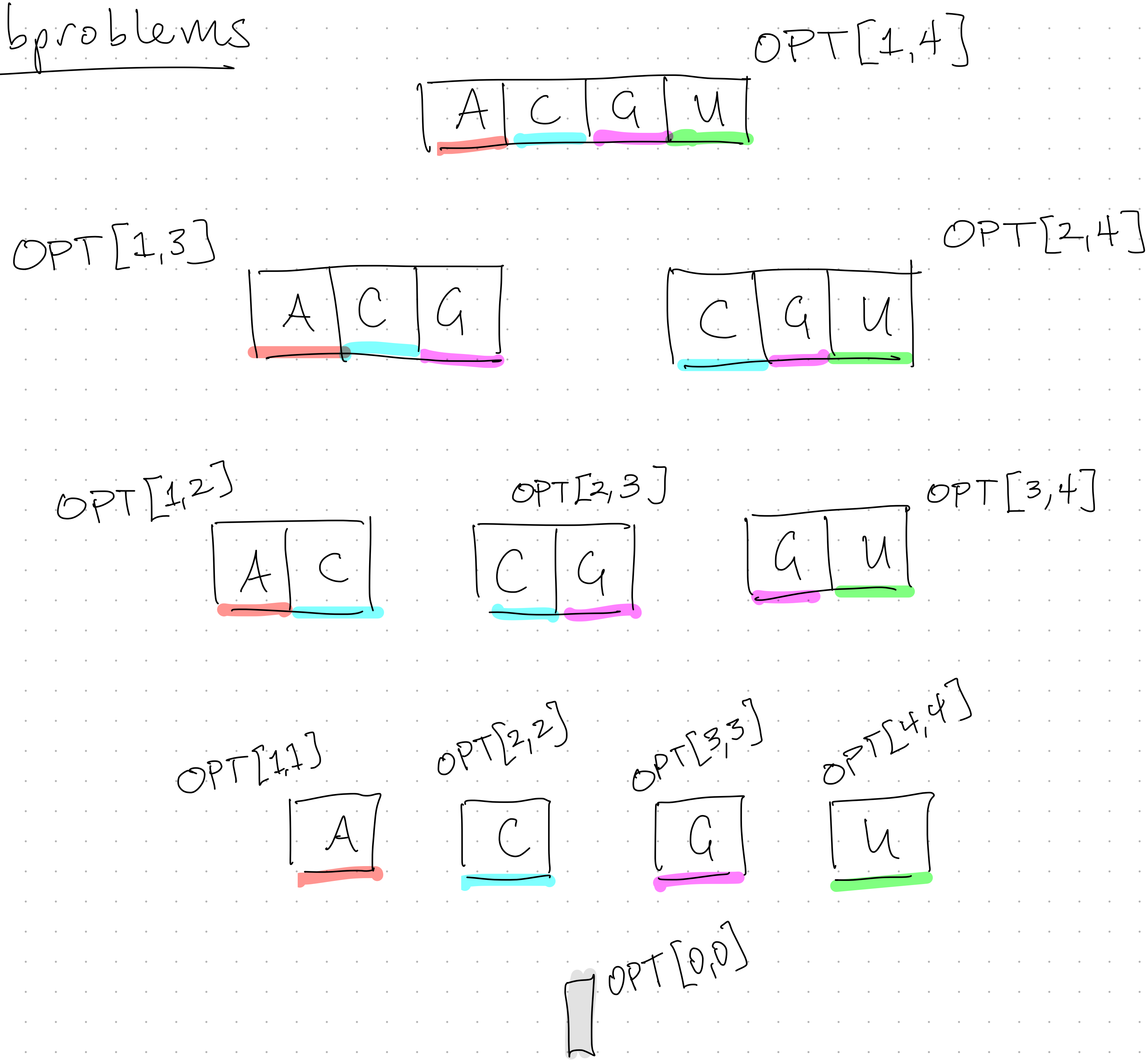
$$OPT[p, r] = 0 \quad \text{if } p \geq r$$

$$OPT[p, r] = \max \begin{cases} OPT[p, r-1], \\ \max\limits_{\substack{q \in [p, r-1] \\ (M_q, M_r) \in B}} \{ 1 + OPT[p, q-1] + OPT[q+1, r] \} \end{cases} \quad \text{if } p < r.$$

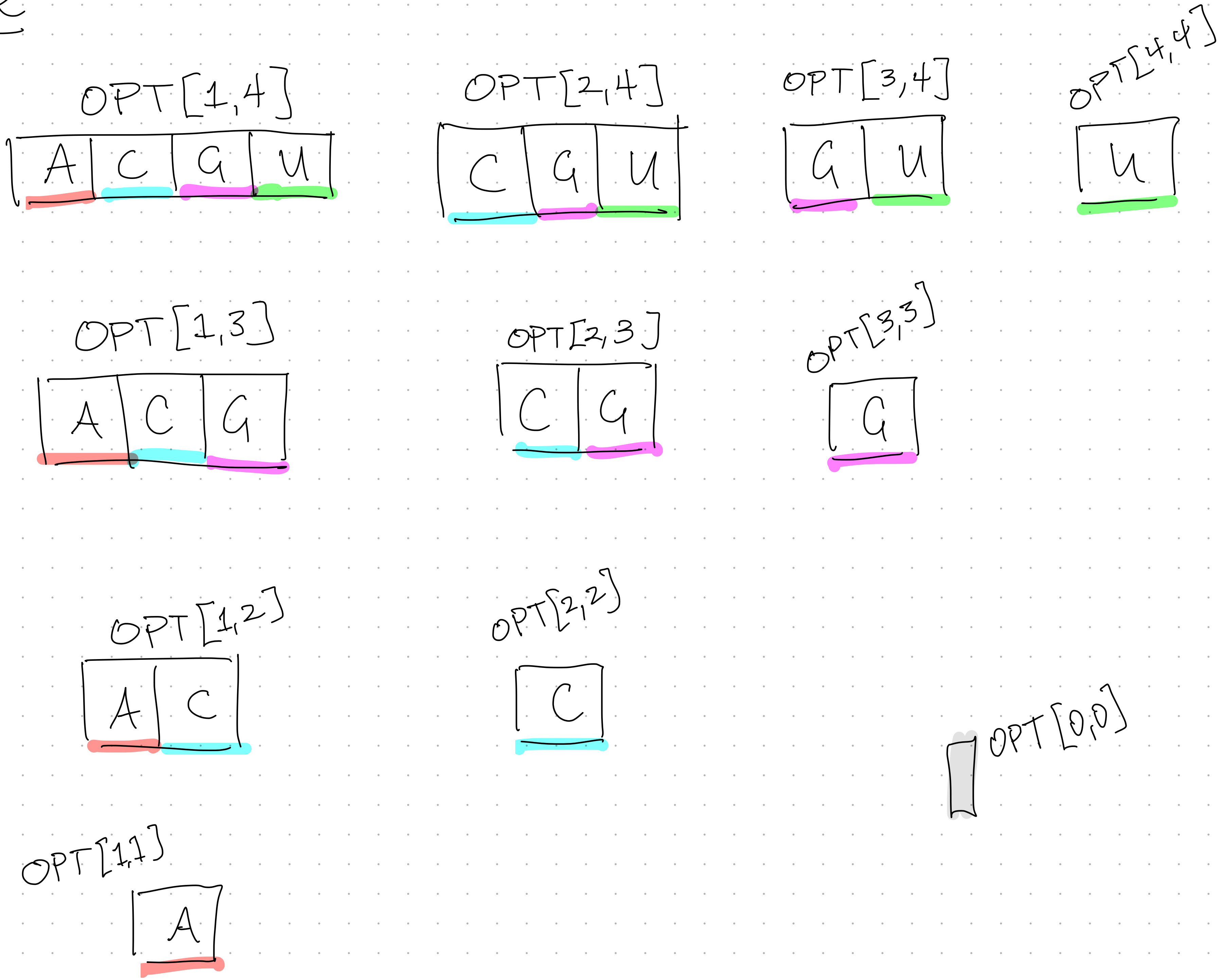
Subproblems



Subproblems



Table


OPT[1,4]
A C G U
OPT[2,4]
C G U
OPT[3,4]
G U
OPT[4,4]
U
OPT[1,3]
A C G
OPT[2,3]
C G
OPT[3,3]
G
OPT[1,2]
A C
OPT[2,2]
C
OPT[0,0]
OPT[1,1]
A

Table

OPT[1,4] A C G U	OPT[2,4] C G U	OPT[3,4] G U	OPT[4,4] U
OPT[1,3] A C G	OPT[2,3] C G	OPT[3,3] G	
OPT[1,2] A C	OPT[2,2] C		OPT[0,0]
OPT[1,1] A			

Proof of Correctness. By induction on the width of interval considered in OPT.

Base Case. $w=0$, $w=1$.

$OPT[p,p]=0$ $\quad$ $OPT[p,p+1]=0$

// There are zero possible matchings between 0 and 1 characters. ✓

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Inductive Step

IH: $\forall$ widths $w < w_0$. $\forall r \in [w+1, n]$

$OPT[r-w, r] =$ Max feasible non-crossing base pairs from $[r-w, r]$

Proof of Correctness. By induction on the width of interval considered in OPT.

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Inductive Step IH: $\forall w < w_0 \;\; \forall r \in [w+1, n]$, $OPT[r-w, r]$ = Max non-crossing base pairs.

We show our recurrence considers all feasible base pairings and takes the maximum.

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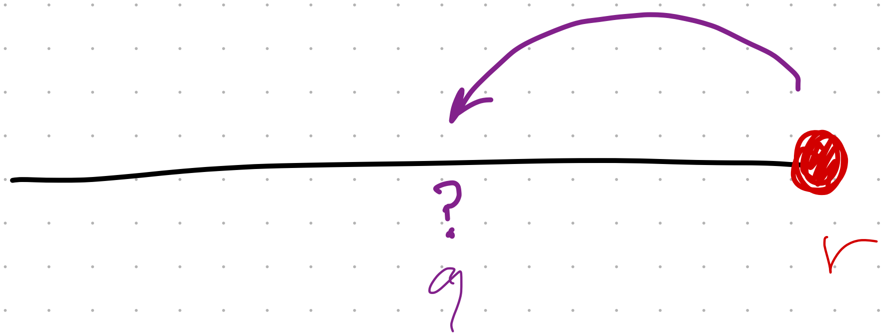
We show our recurrence considers all feasible base pairings, and takes the maximum.

Case 1: M_r NOT involved $\Rightarrow$ $OPT[r-w, r-1]$ is optimal (already computed)

Case M_r is involved.

Recurrence considers all feasible matches in BP for M_r



Suppose we find and match M_r to some M_q.

Then, by non-crossing

No base pairs are allowed with endpoints

$$(p, p') \text{ s.t. } \quad p < q < p' < r.$$

$\Rightarrow$ all remaining feasible solns. have matches between

$$[1 \to q-1] \text{ and } [q+1 \to r-1].$$

Our Recurrence Reflects this.

RNA-Fold(m)

For $p = 1 \to n$: $OPT[p, p] = 0$.

For width $= 1 \to n-1$ // for each width

For $p = 1 \to n -$ width // go through each window $[p, r]$ of the width

$r = p +$ width

RNA-Fold (n)

For $p = 1 \to n$: $OPT[p, p] = 0$.

For width $= 1 \to n-1$

  For $p = 1 \to n - \text{width}$

    $r = p + \text{width}$

    prev $= OPT[p, r-1]$

    match $= 0$

    → pick best match

$$OPT[p, r] = \max \{ \text{prev}, \text{match} \}$$

RNA-Fold(m)

```
For p = 1 → n : OPT[p, p] = 0.

For width = 1 → n-1
    For p = 1 → n - width
        r = p + width
        prev = OPT[p, r-1]
        match = 0
        For q = p → r-1
        |   if (M_q, M_r) ∈ BP :
        |       match = max { match, 1 + OPT[p, q-1]
        |                            + OPT[q+1, r] }
        OPT[p, r] = max { prev, match }
```

RNA-Fold(m)

For $p = 1 \to n$: $OPT[p,p] = 0$.

Running Time?

For width $= 1 \to n-1$

  For $p = 1 \to n - \text{width}$

    $r = p + \text{width}$

    prev $= OPT[p, r-1]$

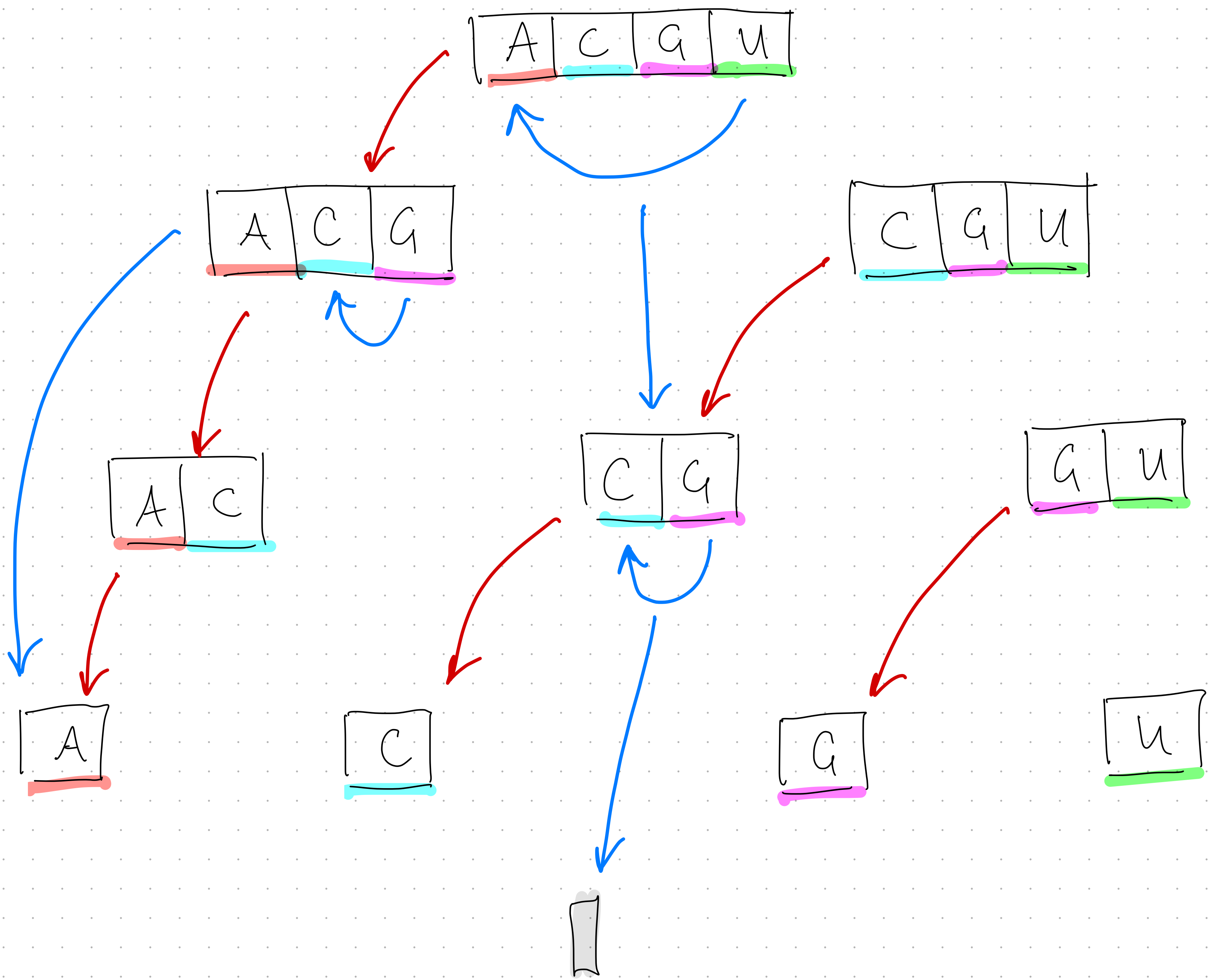
    match $= 0$

    For $q = p \to r-1$

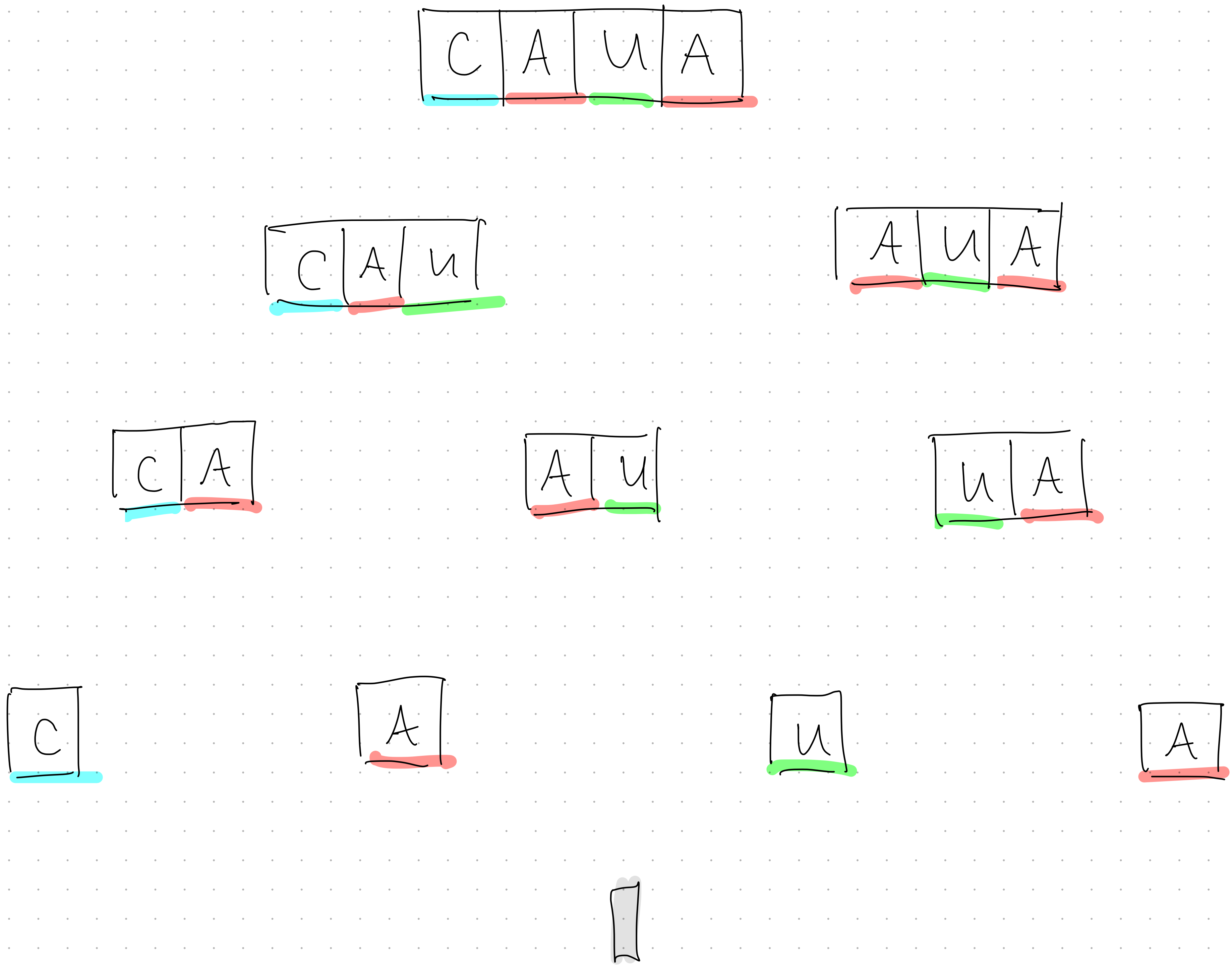
      if $(M_q, M_r) \in BP$:

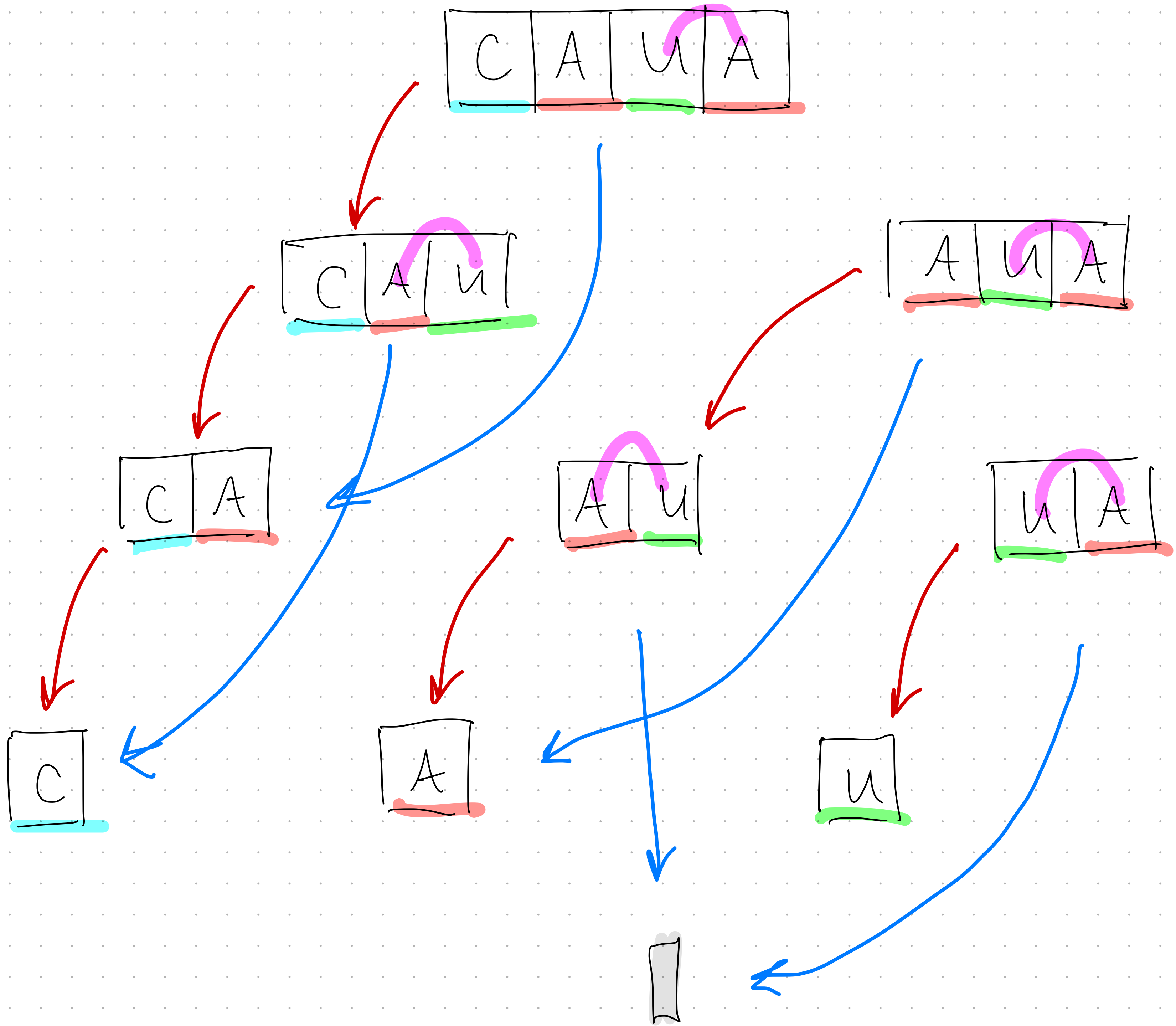
        match $= \max \left\{ \text{match}, \; \begin{array}{l} 1 + OPT[p, q-1] \\ + OPT[q+1, r] \end{array} \right\}$

    $OPT[p, r] = \max \{ \text{prev}, \text{match} \}$

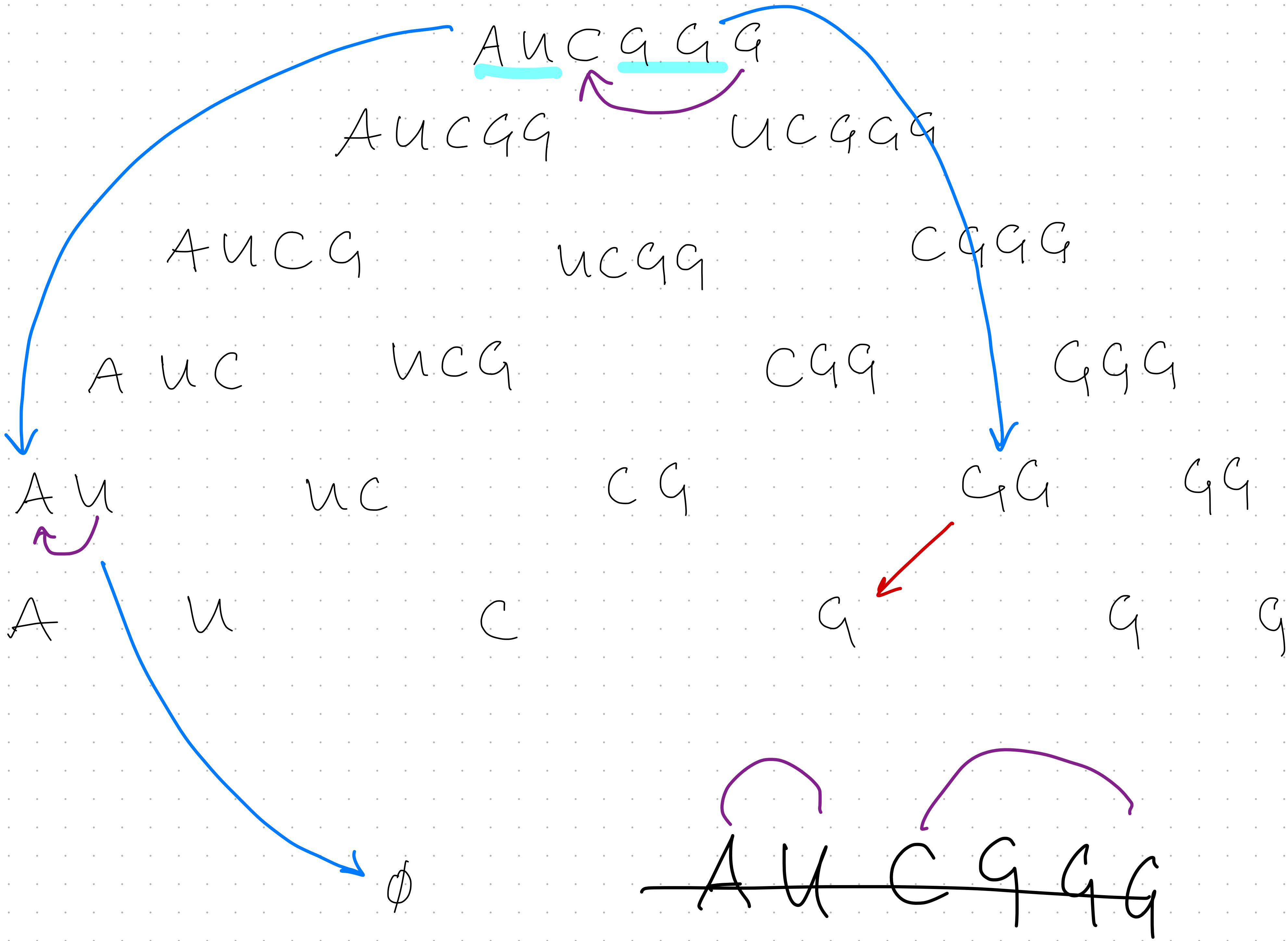


A C G U
A C G
C G U
A C
C G
G U
A
C
G
U


C A U A
C A U
A U A
C A
A U
U A
C
A
U
A



C A U A
C A U
A U A
C A
A U
U A
C
A
U
A


AUCGGG
AUCGG
UCGGG
AUCG
UCGG
CGGG
AUC
UCG
CGG
GGG
AU
UC
CG
GG
GG
A
U
C
G
G
G
∅
AUCGGG

$OPT[1,4]$

$OPT[1,3]$ $OPT[2,4]$

$OPT[1,2]$ $OPT[2,3]$ $OPT[3,4]$

$OPT[1,1]$ $OPT[2,2]$ $OPT[3,3]$ $OPT[4,4]$

$\emptyset$

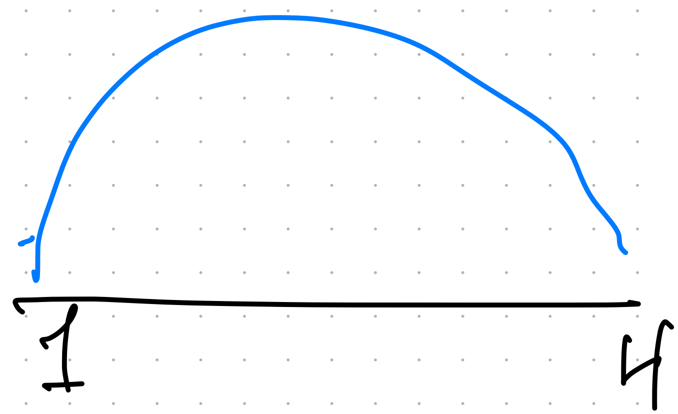
$OPT[1,4]$

$OPT[1,3]$ $\quad$ $OPT[2,4]$

$OPT[1,2]$ $\quad$ $OPT[2,3]$ $\quad$ $OPT[3,4]$

$OPT[1,1]$ $\quad$ $OPT[2,2]$ $\quad$ $OPT[3,3]$ $\quad$ $OPT[4,4]$

$\emptyset$



RNA-Fold(m)

$$\underbrace{\text{BACK}[p,r]}_{\text{which subproblems yield } OPT[p,r]}$$

For $p = 1 \to n$: $OPT[p,p] = 0$.

For width $= 1 \to n-1$

  For $p = 1 \to n - \text{width}$

    $r = p + \text{width}$

    prev $= OPT[p, r-1]$

    match $= 0$

    For $q = p \to r-1$

      if $(M_q, M_r) \in BP$:

        $$\text{match} = \max \left\{ \text{match},\ 1 + OPT[p, q-1] + OPT[q+1, r] \right\}$$

    $OPT[p,r] = \max\{\text{prev}, \text{match}\}$

RNA-Fold(M)

For $p = 1 \to n$: $OPT[p,p] = 0$.

For width $= 1 \to n-1$

  For $p = 1 \to n - \text{width}$

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$\underbrace{BACK[p,r]}_{\text{which subproblems yield } OPT[p,r]}$

$BACK[p,r] = r-1$

RNA-Fold(m)

For $p = 1 \to n$: $OPT[p, p] = 0$.

For $width = 1 \to n-1$

  For $p = 1 \to n - width$

    $r = p + width$

    $prev = OPT[p, r-1]$

    $match = 0$

    For $q = p \to r-1$

      if $(M_q, M_r) \in BP$.

        $match = \max \left\{ match, \; 1 + OPT[p, q-1] + OPT[q+1, r] \right\}$

    $OPT[p, r] = \max \{ prev, match \}$

$\underbrace{BACK[p, r]}_{\text{which subproblems yield } OPT[p,r]}$

$BACK[p, r] = r-1$

$BACK[p, r] = q$

from last update