COMP1730/COMP6730
Programming for Scientists

Dynamic programming

Outline

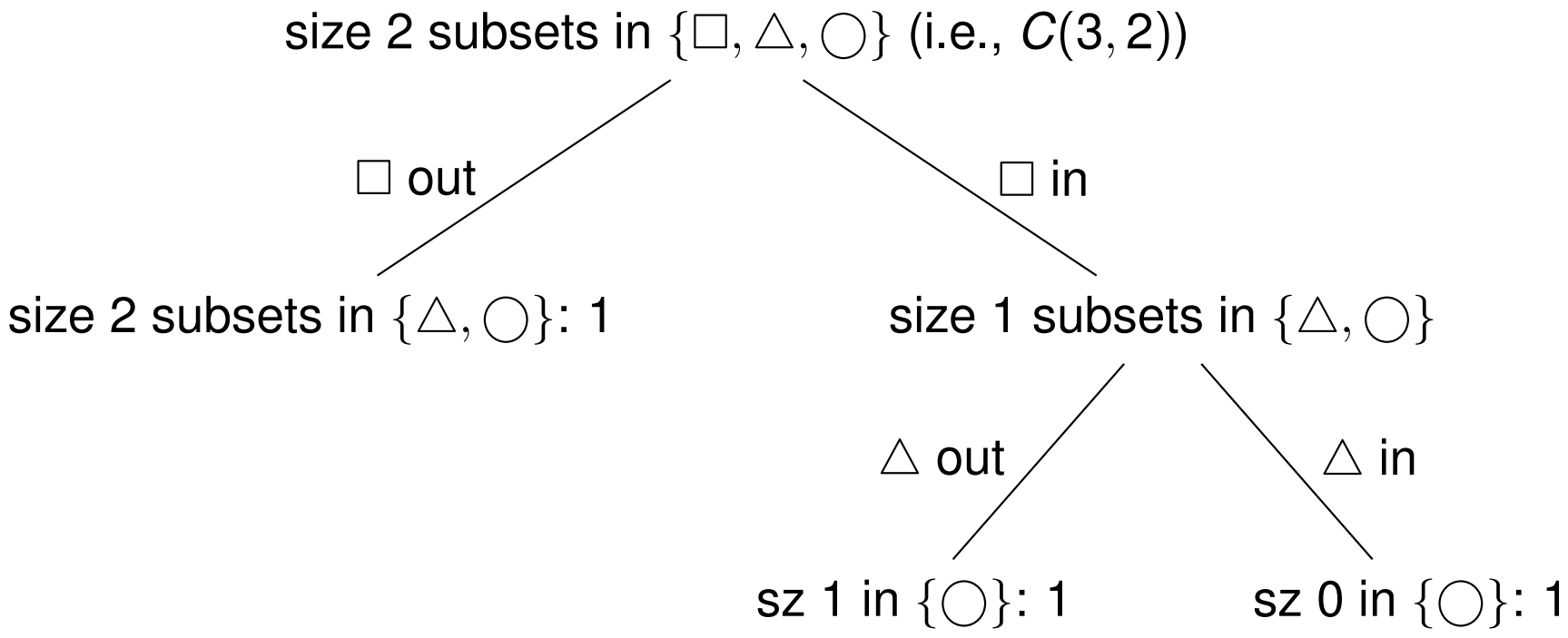
* **Dynamic programming**
* (DNA) sequence alignment

Recursion or iteration?

* Examples of problems that could be solved both with recursion and with iteration:
  - Counting boxes in a stack
  - Solving an equation (the interval-halving algorithm)
* Examples of problems for which we have only seen recursive solutions for:
  - Counting how many different subsets of size k are there in a set of size n (denoted as $C(n, k)$; revisited next)
  - Sudoku problem
  - The subset sum problem (a.k.a. “knapsack problem”): Given n integers $w_1, \ldots, w_n$, and an integer C, is there a subset of them that sums to exactly C?

Example: Counting subsets of size k

* Compute number of different subsets with k elements (i.e., of size k) in a set with n elements ($n \geq k \geq 0$)
* Denoted as $C(n, k)$ (example with $n = 3$, $k = 2$)



Recursive formulation (recap)

* Simple recursive formulation:

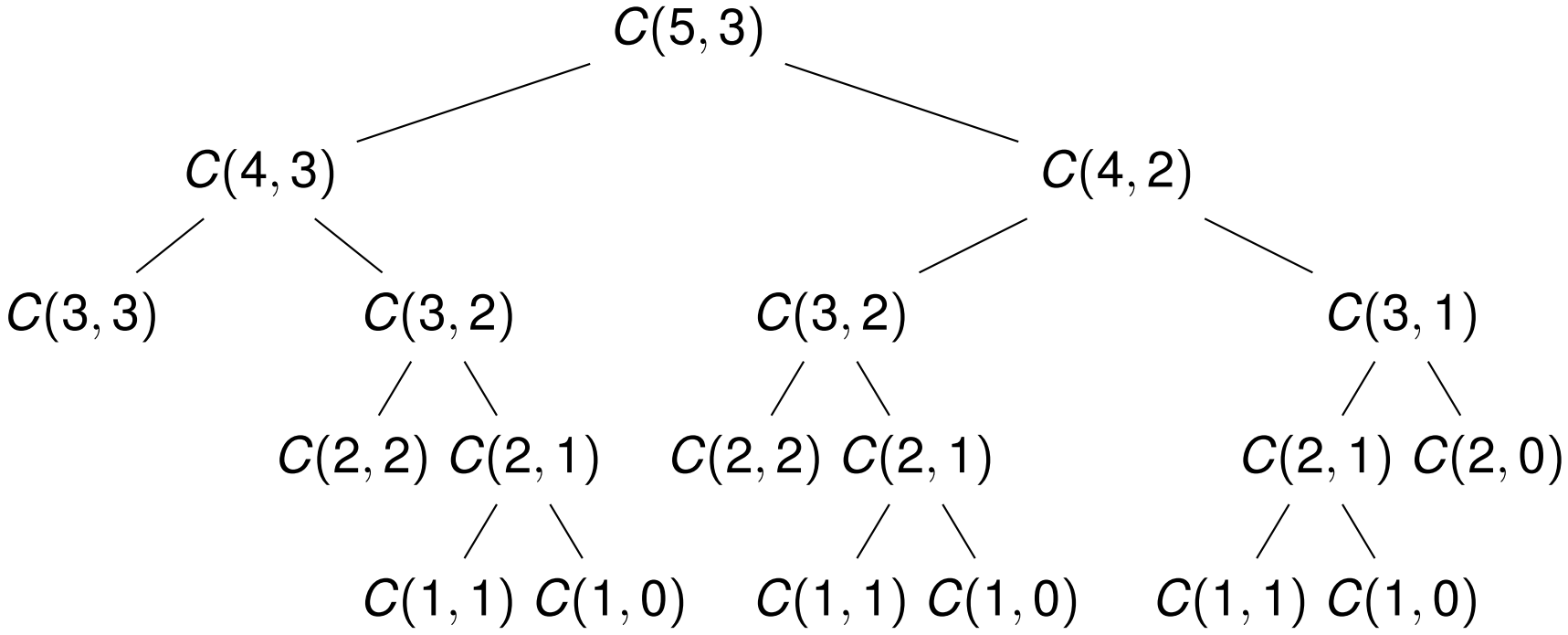
$$C(n,k) = C(n-1,k) + C(n-1,k-1)$$
$$C(n,0) = 1$$
$$C(n,n) = 1$$

* Simple recursive implementation:

```
def C(n, k):
    if k == n or k == 0:
        return 1  # base cases
    else:
        return C(n-1, k) + C(n-1, k-1)
```

* Is it possible to implement $C(n,k)$ with iteration? (yes, next slides)

Call tree for $C(5,3)$

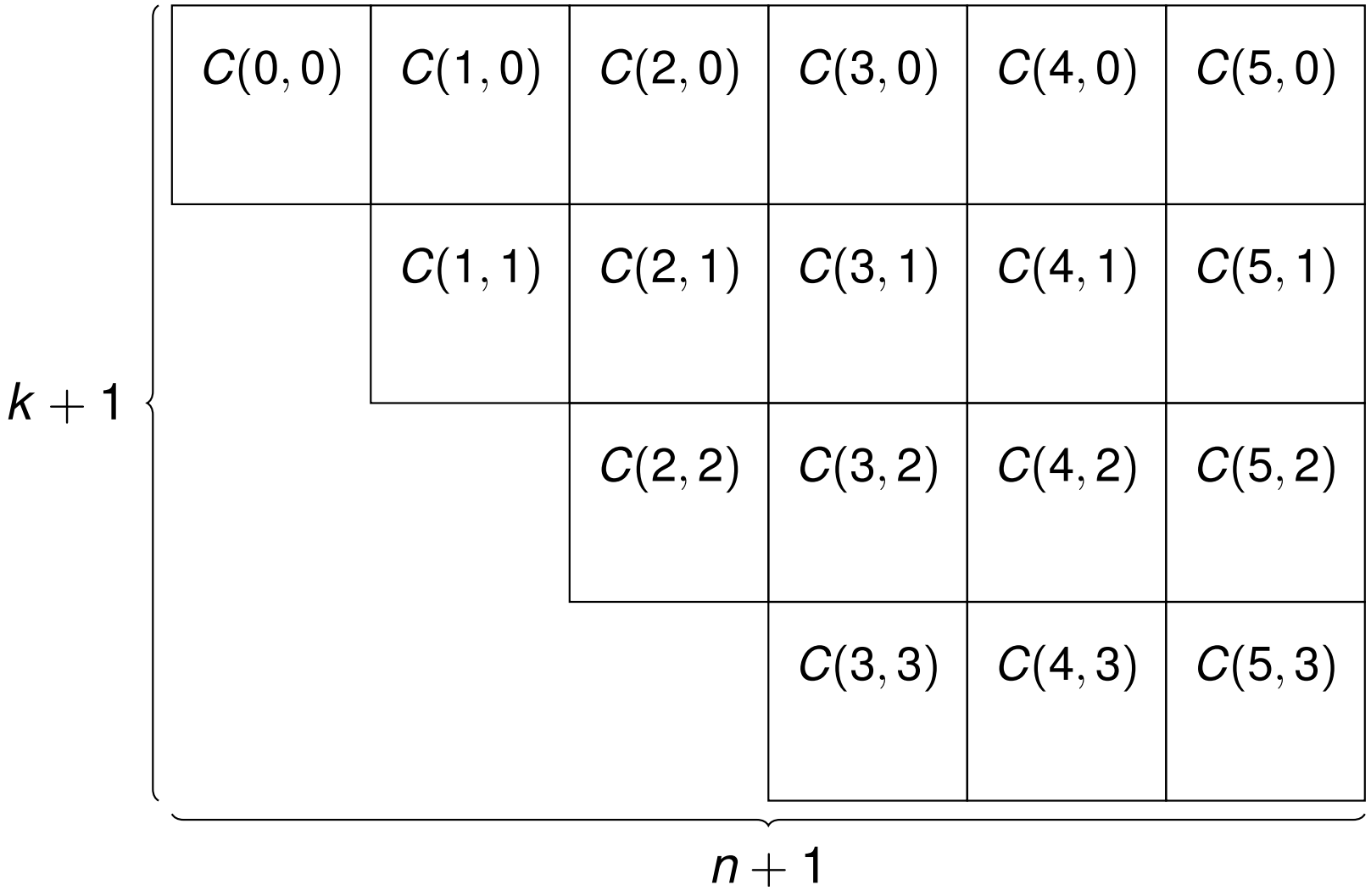


Note repeated work

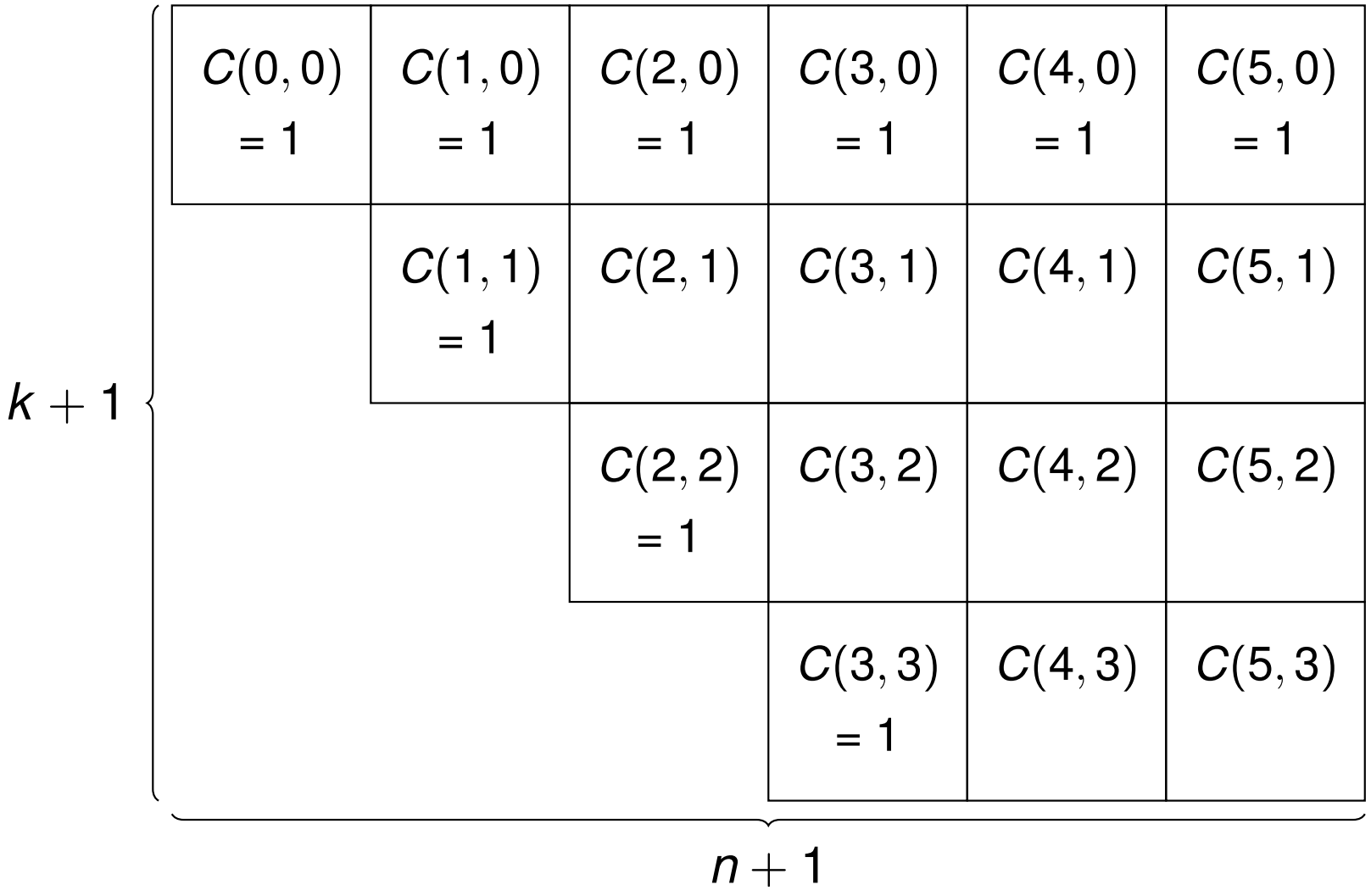
Dynamic programming (basic idea)

* The idea of **dynamic programming** is to store answers to (recursively defined) subproblems, to avoid computing them repeatedly
* Trade memory for computation time: at the price of extra memory we (significantly) reduce number of operations
* By computing subproblem solutions “from the bottom up”, we can also transform a recursive algorithm into an iterative one:
  - solve the base cases first;
  - then, repeatedly, solve problems whose subproblems are already solved;
  - repeat until the whole problem is solved
* Need a way to index stored solutions to subproblems

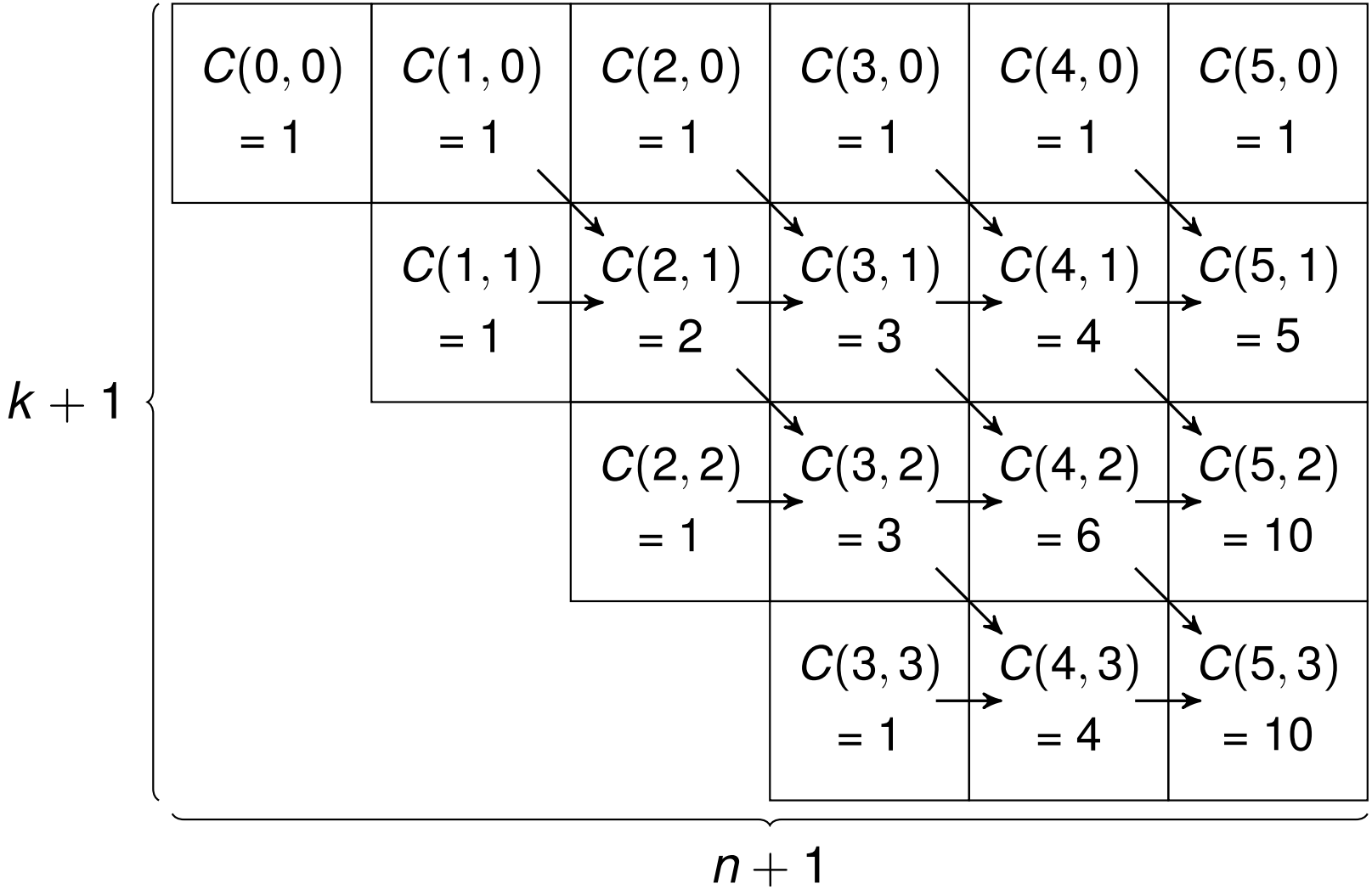
2D array with subproblem solutions



With base cases solved



Complete remaining subproblems



Outline

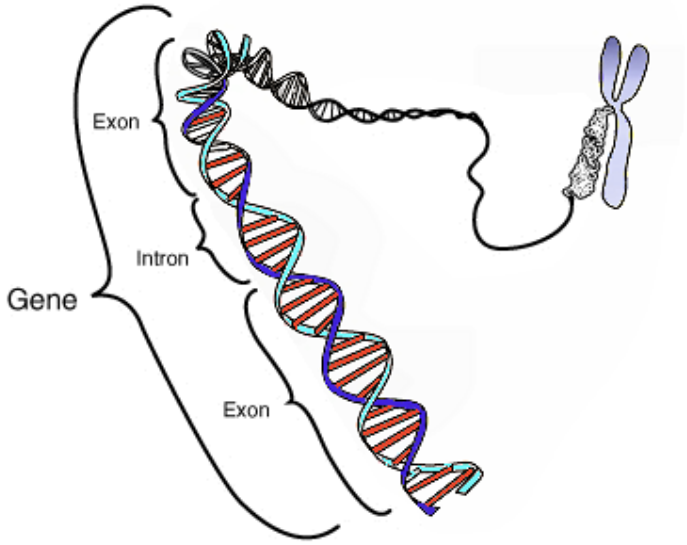
* Dynamic programming
* **(DNA) sequence alignment**

BRCA 1 gene

CTTAGCGGTAGCCCCTTGGTTTCCGTGGCAACGGAAAAGCGCGGGAATTACAGATAAATTAAAACTGCGACTGCGCGGCGTGAGCTCGC
TGAGACTTCCTGGACGGGGGACAGGCTGTGGGGTTTCTCAGATAACTGGGCCCCTGCGCTCAGGAGGCCTTCACCCTCTGCTCTGGTTC
ATTGGAACAGAAAGAAATGGATTTATCTGCTCTTCGCGTTGAAGAAGTACAAAATGTCATTAATGCTATGCAGAAAATCTTAGAGTGTC
CCATCTGTCTGGAGTTGATCAAGGAACCTGTCTCCACAAAGTGTGACCACATATTTTGCAAATTTTGCATGCTGAAACTTCTCAACCAG
AAGAAAGGGCCTTCACAGTGTCCTTTATGTAAGAATGATATAACCAAAAGGAGCCTACAAGAAAGTACGAGATTTAGTCAACTTGTTGA
AGAGCTATTGAAAATCATTTGTGCTTTTCAGCTTGACACAGGTTTGGAGTATGCAAACAGCTATAATTTTGCAAAAAAGGAAAATAACT
CTCCTGAACATCTAAAAGATGAAGTTTCTATCATCCAAAGTATGGGCTACAGAAACCGTGCCAAAAGACTTCTACAGAGTGAACCCGAA
AATCCTTCCTTGGAAACCAGTCTCAGTGTCCAACTCTCTAACCTTGGAACTGTGAGAACTCTGAGGACAAAGCAGCGGATACAACCTCA
AAAGACGTCTGTCTACATTGAATTGGGATCTGATTCTTCTGAAGATACCGTTAATAAGGCAACTTATTGCAGTGTGGGAGATCAAGAAT
TGTTACAAATCACCCCTCAAGGAACCAGGGATGAAATCAGTTTGGATTCTGCAAAAAAGGCTGCTTGTGAATTTTCTGAGACGGATGTA
ACAAATACTGAACATCATCAACCCAGTAATAATGATTTGAACACCACTGAGAAGCGTGCAGCTGAGAGGCATCCAGAAAAGTATCAGGG
TGAAGCAGCATCTGGGTGTGAGAGTGAAACAAGCGTCTCTGAAGACTGCTCAGGGCTATCCTCTCAGAGTGACATTTTAACCACTCAGC
AGAGGGATACCATGCAACATAACCTGATAAAGCTCCAGCAGGAAATGGCTGAACTAGAAGCTGTGTTAGAACAGCATGGGAGCCAGCCT
TCTAACAGCTACCCTTCCATCATAAGTGACTCTTCTGCCCTTGAGGACCTGCGAAATCCAGAACAAAGCACATCAGAAAAAGCAGTATT
AACTTCACAGAAAAGTAGTGAATACCCTATAAGCCAGAATCCAGAAGGCCTTTCTGCTGACAAGTTTGAGGTGTCTGCAGATAGTTCTA
CCAGTAAAAATAAAGAACCAGGAGTGGAAAGGTCATCCCCTTCTAAATGCCCATCATTAGATGATAGGTGGTACATGCACAGTTGCTCT
GGGAGTCTTCAGAATAGAAACTACCCATCTCAAGAGGAGCTCATTAAGGTTGTTGATGTGGAGGAGCAACAGCTGGAAGAGTCTGGGCC
ACACGATTTGACGGAAACATCTTACTTGCCAAGGCAAGATCTAGAGGGAACCCCTTACCTGGAATCTGGAATCAGCCTCTTCTCTGATG
ACCCTGAATCTGATCCTTCTGAAGACAGAGCCCCAGAGTCAGCTCGTGTTGGCAACATACCATCTTCAACCTCTGCATTGAAAGTTCCC
CAATTGAAAGTTGCAGAATCTGCCCAGAGTCCAGCTGCTGCTCATACTACTGATACTGCTGGGTATAATGCAATGGAAGAAAGTGTGAG
CAGGGAGAAGCCAGAATTGACAGCTTCAACAGAAAGGGTCAACAAAAGAATGTCCATGGTGGTGTCTGGCCTGACCCCAGAAGAATTTA
TGCTCGTGTACAAGTTTGCCAGAAAACACCACATCACTTTAACTAATCTAATTACTGAAGAGACTACTCATGTTGTTATGAAAACAGAT
GCTGAGTTTGTGTGTGAACGGACACTGAAATATTTTCTAGGAATTGCGGGAGGAAAATGGGTAGTTAGCTATTTCTGGGTGACCCAGTC
TATTAAAGAAAGAAAAATGCTGAATGAG

Biological sequence data

* DNA and RNA
* Protein amino acid sequence
* Arrangement of genes in chromosome / genome



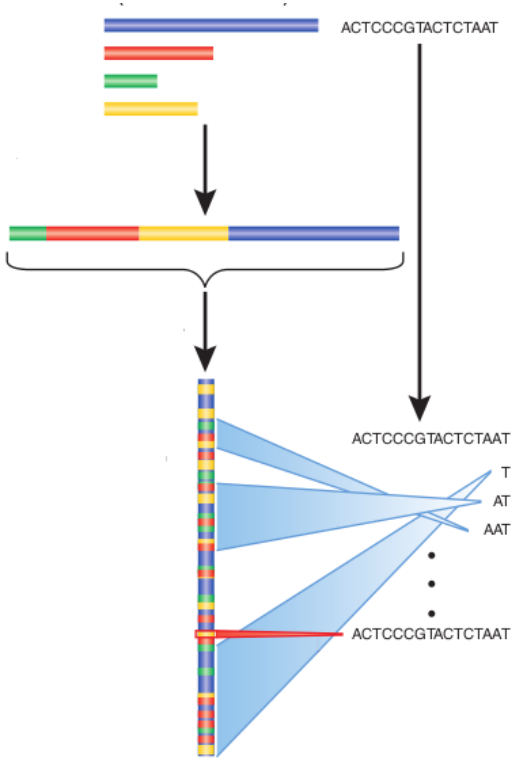
* Human DNA is ~3 billion (i.e., 3×10^9) base pairs
* BRCA 1 & 2 genes are ~80kb (incl. exons)
* Harmful mutations change as few as 2 bases
* DNA sequencer reads are 100–2k bases

* Alignment

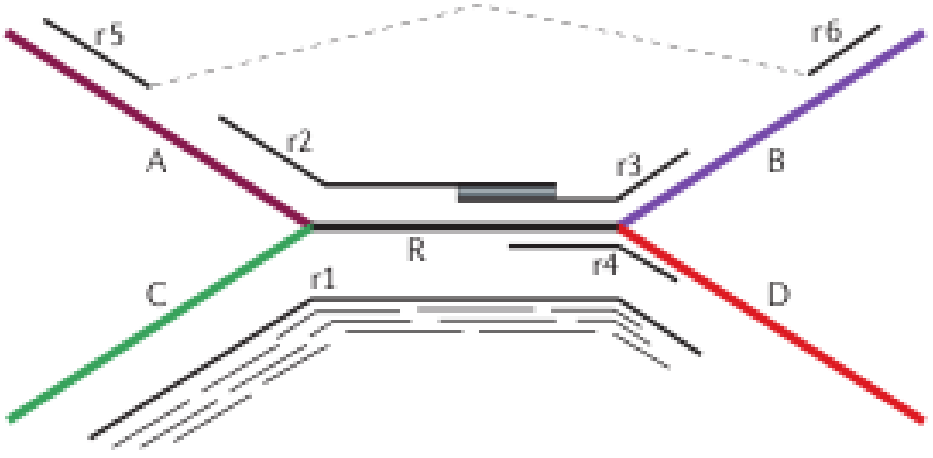
```
GAATTCAG  GAATTCAG
|  |  ||  |  |  ||  |  |
GGA-TC-G  GCAT-C-G

GAATTC-A  GAATTC-A
|  |  ||  |  |  ||  |  |
GGA-TCGA  GCAT-CGA
```

* Mapping



* Assembly



Edit distance

* Minimum (weighted) number of “edit operations” needed to transform one sequence (source) into the other (target)
* Levenshtein (string edit) distance. Edit operations:
  - **Insert** a character (gap in source string)
  - **Delete** a character (gap in target string)
  - **Substitute** a character
* Minimum edit distance equals to the “score” of best sequence alignment

Levenshtein edit distance (example)

* distance(GAATTCA, GGATCGA) = 3
* Edits:

		G A A T T C A
(subst. 1 G)	$\Rightarrow$	G G A T T C A
(del 4)	$\Rightarrow$	G G A T C A
(ins 5 G)	$\Rightarrow$	G G A T C G A

* Alignment (score$=$ 3):

G	**A**	A	T	T	C	_	A
G	**G**	A	T	_	C	G	A
	+1			+1		+1	

Recursive formulation (definition)

$$\text{dist}(s, '\,') = \text{len}(s) * w_{\text{gap}}$$
$$\text{dist}('\,', t) = \text{len}(t) * w_{\text{gap}}$$

$$\text{dist}(s + x, t + y) =$$
$$\min \begin{cases} \text{dist}(s, t) + \begin{cases} 0 & \text{if} x = y \\ w_{\text{sub}} & \text{otherwise} \end{cases} \\ \text{dist}(s + x, t) + w_{\text{gap}} \\ \text{dist}(s, t + y) + w_{\text{gap}} \end{cases}$$

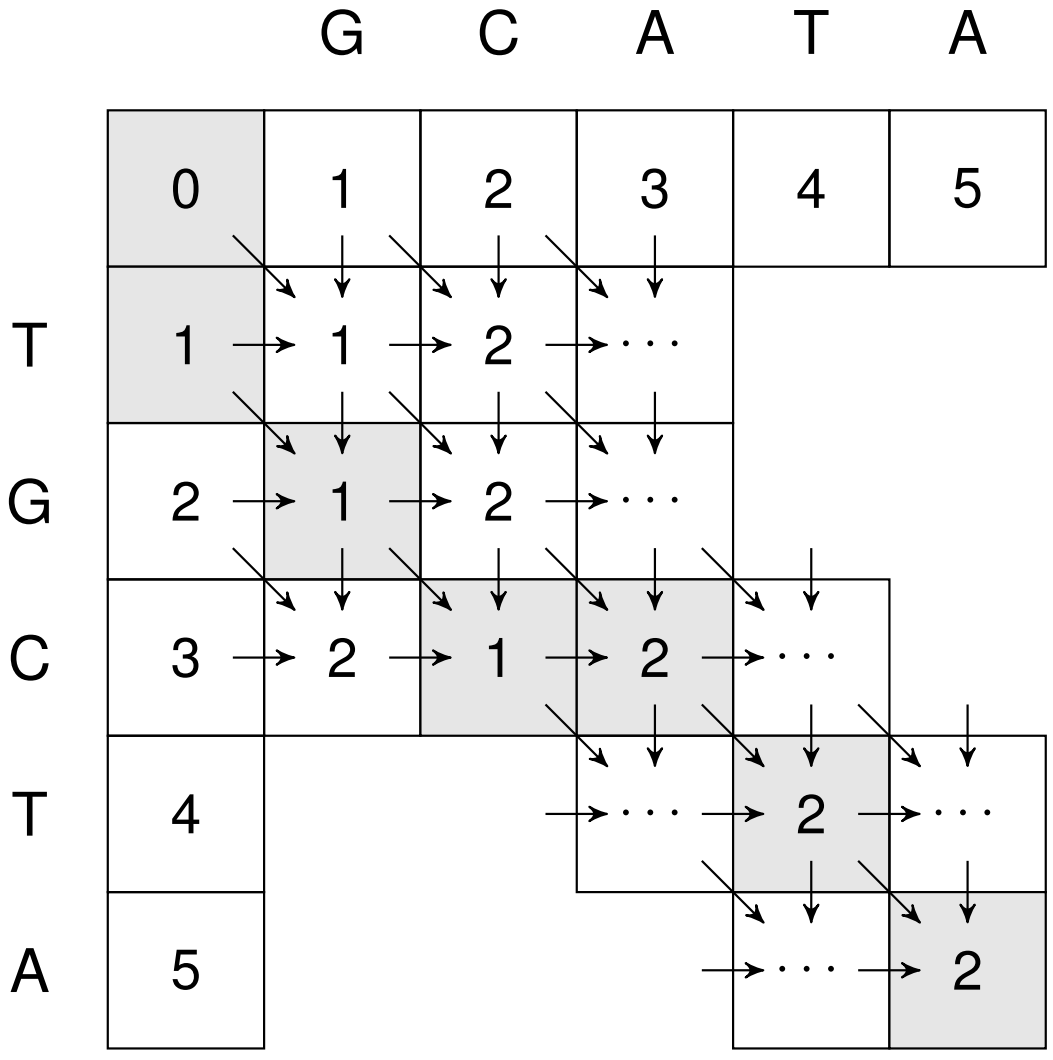
Recursive formulation (implementation)

```
def edit_distance(s, t, w_gap = 1, w_sub = 1):
    """
    Returns the edit distance between 2 sequences
    s and t with gap cost w_gap and substitution
    cost w_sub
    """
    if len(s) == 0:
        return len(t) * w_gap
    elif len(t) == 0:
        return len(s) * w_gap
    else:
        if s[-1] == t[-1]:
            d1 = edit_distance(s[:-1], t[:-1])
        else:
            d1 = edit_distance(s[:-1], t[:-1]) + w_sub
        d2 = edit_distance(s, t[:-1]) + w_gap
        d3 = edit_distance(s[:-1], t) + w_gap
        return min(d1, d2, d3)
```

Dynamic programming formulation (sketch)

* How to index stored solutions to subproblems?
  - 2D array of shape `(len(s)+1, len(t)+1)`
  - (i, j): `edit_distance(s[:i], t[:j])`
* Base cases?
  - One of the two sequences is empty ($i = 0$ or $j = 0$)
* Update: (i, j) is equal to minimum of:
  - $(i - 1, j - 1)$ (plus subst. weight if `s[i-1] != t[j-1]`)
  - $(i - 1, j)$ plus gap weight
  - $(i, j - 1)$ plus gap weight

Dynamic programming formulation (dynamics)



Takehome messages

* Dynamic programming is an algorithmic paradigm that can be used to solve optimization problems in polynomial time for which brute-force approaches (e.g., recursion) may result in exponential time
* It comes at a price: increased memory consumption
* Applicable to many different problems, but not always
* The optimization problem has to have (or should be recasted to have) the property that the optimal solution can be expressed as a combination of optimal solutions to **overlapping** subproblems