Common Substrings in Random Strings

Eric Blais, Mathieu Blanchette McGill Centre for Bioinformatics [eblais,blanchem]@mcb.mcgill.ca

Common *k*-Substring Problem

- Given: A set of strings $S_1, S_2, ..., S_r$ and a length k,
- **Determine**: If there is a string T of length k that is a substring of each of S₁, S₂, ..., S_r

Common k-Substring Problem

CTTGCTTAGTCTTTTGCTGTGTGCTAATGTTTCGAAATGT CTCAGCTAATCTGCGAGAGAGCTTCAGGGGGCGACAATCTACG AGTGCATACAGACTCTAATACCAAATTGTGGAACACCATC TGGATAGACTATTCCCCGGTTATTACCGCTAATGGAGTCGT CAGGAATATGTATCTCATACCCCGGCTAATAAGGGTTAGA ACAAAAGGAAGCGGCGGCTTGACGTGTACCTAATGATCGT TCTAATGGAACGGGGGCACTTCGGCTAAATACAGGGAGAGT TGTCACATCTAATTTCTACCTTACGACCGTCTCGAGTAGC TAAACTTGCACTAACCTAATTGTCTGGGGTTTGGGAGAGCG GGCATGCCCCGATGCTGTGTGTAGCCCTAATAGACCGGATAA

Common k-Substring Problem

CTTGCTTAGTCTTTTGCTGTGTGCTAATGTTTCGAAATGT CTCAGCTAATCTGCGAGAGAGCTTCAGGGGGCGACAATCTACG AGTGCATACAGACTCTAATACCAAATTGTGGAAACACCATC TGGATAGACTATTCCCCGGTTATTACCGCTAATGGAGTCGT CAGGAATATGTATCTCATACCCCGGCTAATAAGGGTTAGA ACAAAAGGAAGCGGCGGCGTTGACGTGTACCTAATGATCGT TCTAATGGAACGGGGGCACTTCGGCTAAATACAGGGAGAGT TGTCACATCTAATTTCTACCTTACGACCGTCTCGAGTAGC TAAACTTGCACTAACCTAATGTCTGGGGTTTGGGAAGAGCG GGCATGCCCCGATGCTGTGTGTAGCCCTAATAGACCGGATAA

Common *k*-Substring in Random Strings (CSRS) Problem

- **Given**: A random process P that generates set of strings $S_1, S_2, ..., S_r$ and a length k,
- Find: The probability that there is a string T of length k that is a substring of each of S₁, S₂, ..., S_r

History of the CSRS Problem

- Study began 20+ years ago, when Arratia & Waterman examined the asymptotic behavior of the length of the longest perfect alignment between two random strings.
- Results to date offer good approximation when the number of random strings is **low**, but poor approximations when there are many random strings in the problem instance.

New Approximations to the CSRS Problem

- We present 2 new approximations for the CSRS problem, aimed specifically at being accurate when there are many random strings:
 - 1. Independent Words Model
 - 2. Double Independence Model

• Independent Words Assumption: Different *k*-substrings occur independently of each other in a random string

• Resulting approximation:

$$P(\zeta) = 1 - \prod_{w \in \Sigma^k} (1 - P(\xi_w)^r)$$

• Notation:

 $P(\xi_w)$ – Probability of the string w occurring in a random string

 $P(\zeta)$ – Probability that at least one string of length k occurs as a common substring to all the random strings

Table 1: Approximations to CSRS for k = 6, in *r* random strings of length *n* generated by a Bernoulli process.

r	п	Indep. Words Approx.	Monte-Carlo Est.
2	18	0.0490	0.0386
4	197	0.0497	0.0477
6	467	0.0499	0.0490
8	727	0.0500	0.0493
10	958	0.0501	0.0495
2	11	0.0107	0.0088
4	131	0.0100	0.0096
6	346	0.0099	0.0098
8	569	0.0100	0.0099
10	774	0.0100	0.0100

- Time complexity: $O(\sigma^k)$
 - Where σ is the size of the input alphabet
- Observation: We can reduce the time complexity by grouping together strings that have the same probability of occurrence in random strings

Double Independence Model

- Assumption 1: Different *k*-substrings occur independently of each other in random strings
- Assumption 2: The self-overlap structure of a *k*-substring can be ignored when calculating the probability that it occurs in a random string

Double Independence Model

- Approach:
 - Define the *composition* for strings of length k such that strings that share the same composition have the same probability of occurring in a random string
 - 2. Enumerate every composition for strings of length *k*.

Double Independence Model

• Resulting approximation:

$$P(\zeta) = 1 - \prod_{\gamma \in \mathcal{C}_k} (1 - P_{\gamma}^{r})^{\Omega(\gamma)}$$

- Notation:
 - C_k Set of all compositions for strings of length k
 - P_{γ} Probability of occurrence for strings with composition γ

 $\Omega(\gamma)$ – Number of strings with the composition γ

- The *Bernoulli composition* of a string *w* is the multiset γ of characters in *w*.
 - Example: The composition of the string ACCATA is $\gamma = \{A, A, A, C, C, T\}$

$$P(\zeta) = 1 - \prod_{\gamma \in \mathcal{C}_k} (1 - P_{\gamma}^{r})^{\Omega(\gamma)}$$

- The probability P_{γ} can be computed easily
- Enumeration of the compositions in C_k can be accomplished with a simple recursive algorithm
- Number of strings with the composition γ given by multinomial equation.

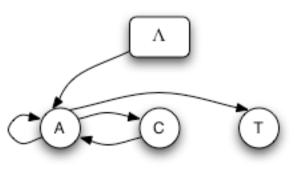
Table 1: Approximations to CSRS for k = 6, in *r* random strings of length *n* generated by a Bernoulli process.

r	п	DIM Approx.	IWM Approx.	Monte-Carlo
2	18	0.0491	0.0490	0.0386
4	197	0.0500	0.0497	0.0477
6	467	0.0508	0.0499	0.0490
8	727	0.0514	0.0500	0.0493
10	958	0.0519	0.0501	0.0495
2	11	0.0107	0.0107	0.0088
4	131	0.0101	0.0100	0.0096
6	346	0.0101	0.0099	0.0098
8	569	0.0103	0.0100	0.0099
10	774	0.0104	0.0100	0.0100

- Time Complexity: $O(k^{\sigma-1})$
- + Running time polynomial in k
- Less accurate than the Independent Words Model

- The *1st-order Markov composition* of a string w is the multiset γ of Markov transitions between adjacent characters in w and between the start state Λ and the first character in w
 - Example: The 1st-order Markov composition of the string AACAT is $\gamma = \{(\Lambda \rightarrow A), (A \rightarrow A), (A \rightarrow C), (A \rightarrow T), (C \rightarrow A)\}$

• The 1st-order Markov composition of a string can also be represented as a directed multigraph.

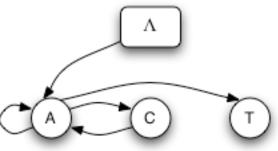


 Example: The 1st-order Markov composition graph of the string AACAT.

$$P(\zeta) = 1 - \prod_{\gamma \in \mathcal{C}_k} (1 - P_{\gamma}^{r})^{\Omega(\gamma)}$$

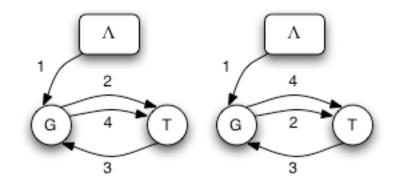
- P_{γ} is easy to compute
- Challenge 1: Counting the number of strings that share the Markov composition γ
- Challenge 2: Enumerating all the compositions in C_k

To count the number of strings with the composition γ, we will count the number of Eulerian trails on the Markov composition graph for γ.



• Counting the number of Eulerian trails on a directed multigraph is done with the BEST theorem [van Aardenne-Ehrenfest and de Bruijn, 1951].

• **But**: some distinct Eulerian trails correspond to the same string,



• Result: The number of strings with the composition γ is defined by

$$\Omega(\gamma) = \frac{\lambda_{\gamma}}{\prod_{(u,v) \in V_{\gamma}^2} M(u,v)!}$$

• Notation:

 λ_{γ} – The number of Eulerian trails on the Markov composition graph γ

M(u, v) – The number of edges going from u to v in the Markov composition graph

Table 1: Approximations to CSRS for k = 6, in *r* random strings of length *n* generated by a 1st-order Markov process.

r	п	DIM	DIM w. Correction	Monte-Carlo
2	17	0.0497	0.0495	0.0388
4	175	0.0522	0.0493	0.0474
6	410	0.0549	0.0493	0.0486
8	633	0.0607	0.0494	0.0493
10	828	0.0674	0.0494	0.0493
2	10	0.0088	0.0088	0.0073
4	117	0.0105	0.0101	0.0098
6	304	0.0113	0.0099	0.0099
8	494	0.0128	0.0099	0.0099
10	666	0.0148	0.0098	0.0099

Generalizations

- The Models can also be modified to handle modifications to the original CSRS problem, including:
 - Searching for common substrings in a subset of the random strings
 - Allowing mismatches in the substring occurrences within the random strings

Future Work

- Providing theoretical bounds on the error introduced by the approximations
- Improving the quality of the approximation when the number of strings is low
- Developing new models with weaker assumptions

Acknowledgements

- Uri Keich
- Members of the McGill Centre for Bioinformatics
- Funding by
 - Andre Courtemanche Fellowship
 - NSERC