A Learning Algorithm for String Assembly

Mark K. Goldberg
Darren T. Lim
Malik Magdon-Ismail
@cs.rpi.edu

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Problem Formulation

Collection of $\lambda$ Original Strings

$\mathcal{P}$ (Fragmentation Process)

Collection of Substrings
Problem Statement

**Plausible String Assembly Problem (PSAP):**
Given a collection of strings $\mathcal{C} = \{s_1, \ldots, s_N\}$, construct a physically plausible superstring.

**Physically Plausible:**

1. Consistent with Input Domain.

2. Consistent with Fragmenting Process.

**Efficiency:** Within the lifetime of the universe.
Our Approach

Consistency with:

1. Input domain: **Learning**.

2. Fragmenting: **Statistical**.

Efficiency: **Learning**.
Assembly Strategies

1. Greedy Merging.

2. Boosted Greedy Merging.

3. Full Enumeration Search.

4. Partial Enumeration Search.
Greedy Merging

Merge the fragments with longest overlap until only one fragment remains.

Example:

1. CATAT ATATC TATA
2. CATATC TATA
3. CATATCTATA

SSP: CATATATC

Greedy merging does not even work for SSP!

–SSP is NP-Hard.
Boosted Greedy Merging

Merge the fragments with the longest certified overlap.
Full Enumeration – The Assembly Tree

ATCGCCT  CCTAT  CTATCG  GCCTTT

ATCGCCT  CCTATCG  GCCTTT

CCTATCGCCT  GCCTTT

CCTATCGCCTTT

Use backtracking coordinates, b, to enumerate.
Partial Enumeration Search

- Full enumeration is practically unfeasible.
- Only enumerate a subset of the paths:
  
  Restricted Backtracking

- Which subset:
  
  Learn the subset
To be learned:

1. $\tau$, $\beta$, $M$;

2. The restricted search space, $\{b\}$. 
We need a training set of the form:

$$D = \{c_i, \tau_i, \beta_i, b_i\}$$

$c_i$: A collection of fragments from the input domain of interest.

$\tau_i, \beta_i, b_i$: The correct values for the particular assembly problem.

It appears that we need an (exponentially slow) oracle to generate learning data.
No need for the exponentially slow oracle:

1. Generate string, $S$, from input domain.

2. Use $\mathcal{P}$ to generate fragments.

3. Obtain correct parameters $\tau_i, \beta_i, b_i$. 
\[ M = \max_i \text{length}(b_i) \]

\[ \beta = \max_i \beta_i \]

\[ \tau = (N - 1) - M - \beta \]

\[ x \in \{b\} \iff x < b_i \quad \text{for some } i \]

The set \( \{\tau, \beta, M, \{b\}\} \) defines the learned assembly algorithm.

**Output:** Set of candidate superstrings.
Statistical Selection

Given a candidate superstring, compute:

**Expected frequency of letters** \((\delta)\)

Compare with

**Observed frequency of letters** \((\Delta)\)

Select the candidate that minimizes the discrepancy:

\[
\kappa = \sum_{a \in \Sigma} (\delta_a - \Delta_a)^2
\]
## Experiments

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Concluding Remarks

1. Learn on one DNA; apply to another DNA.

2. Gaps and Errors.

3. Parametric algorithm design
   — Other parameterizations?


5. Learning on one problem size and scaling up to bigger problem sizes.

6. \( k - \)mer technology.

   www.cs.rpi.edu/~magdon