UNIQUE RECONSTRUCTION FROM SUBSTRINGS

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DNA Storage



String Reconstruction

Reconstruct string from *multiple*, *incomplete* and/or *noisy* observations

Examples:

- Levenshtein's *reconstruction problem* [1]
- Trace reconstruction problem [2]
- *k*-deck problem [3]

[1] V. I. Levenshtein, "Efficient reconstruction of sequences from subsequences or supersequences," J. Combin. Theory, Feb. 2001
[2] T. Batu, S. Kannan, S. Khanna, and A. McGregor, "Reconstructing strings from random traces," in SODA, Society for Industrial and Applied Mathematics, Jan. 2004,.
[3] B. Manvel, A. Meyerowitz, A. Schwenk, K. Smith, and P. Stockmeyer, "Reconstruction of sequences," Discrete Mathematics, 1991.

Torn-Paper Reconstruction



D. Bar-Lev, S. Marcovich, E. Yaakobi, and Y. Yehezkeally, "Adversarial torn-paper codes," in *IEEE ISIT*, 2022. S. Nassirpour, I. Shomorony, and A. Vahid, "Reassembly codes for the chop-and-shuffle channel," in arXiv, 2022. A. N. Ravi, A. Vahid, and I. Shomorony, "Capacity of the torn paper channel with lost pieces," in *IEEE ISIT*, 2021. I. Shomorony and A. Vahid, "Torn-paper coding," *IEEE TIT*, Dec. 2021.

Reconstruction from Substring-Composition

R. Gabrys and O. Milenkovic, "Unique reconstruction of coded sequences from multiset substring spectra," *IEEE TIT*, Jun. 2019.
G. Bresler, M. Bresler, and D. Tse, "Optimal assembly for high throughput shotgun sequencing," *BMC Bioinformatics*, Jul. 2013.
H. M. Kiah, G. J. Puleo, and O. Milenkovic, "Codes for DNA sequence profiles," *IEEE TIT*, Jun. 2016.
S. Marcovich and E. Yaakobi, "Reconstruction of strings from their substrings spectrum," *IEEE TIT*, Jul. 2021.
A. S. Motahari, G. Bresler, and D. N. C. Tse, "Information theory of DNA shotgun sequencing," *IEEE TIT*, Oct. 2013.
Y. Yehezkeally, S. Marcovich, and E. Yaakobi, "Multi-strand reconstruction from substrings," in *IEEE ITW*, 2021.



Partial-Overlap Channel



Probabelistic version of this channel:

Ravi, A. N., Vahid, A., and Shomorony, I. (2022). Coded Shotgun Sequencing. ACM JSAIT, 3(1), 147-159.

Agenda

01

Torn-Paper Channel 02

Substring-Composition Channel Partial Overlap Channel

03

04

Future Directions

Notations

$$[n] = \{0, 1, \dots, n-1\}.$$

$$x \circ y$$
: concatenation of $x, y \in \Sigma^*$.

 ℓ -substring of *x*: substring of length ℓ .



Torn-Paper Channel Single-Strand

Single-Strand Torn-Paper Reconstruction



D. Bar-Lev, S. Marcovich, E. Yaakobi, and Y. Yehezkeally, "Adversarial torn-paper codes," in *IEEE ISIT*, 2022. S. Nassirpour, I. Shomorony, and A. Vahid, "Reassembly codes for the chop-and-shuffle channel," in arXiv, 2022. A. N. Ravi, A. Vahid, and I. Shomorony, "Capacity of the torn paper channel with lost pieces," in *IEEE ISIT*, 2021. I. Shomorony and A. Vahid, "Torn-paper coding," *IEEE TIT*, Dec. 2021.

An (L_{\min}, L_{\max}) -segmentation of $x \in \Sigma^n$ is a multiset $\{\{u_0, u_1, \dots, u_{m-1}\}\}$ of substrings such that: (1) $x = u_0 \circ u_1 \circ \cdots \circ u_{m-1}$. (2) $L_{min} \leq |u_i| \leq L_{max}$ for $0 \leq i < m-1$ and $|u_{m-1}| \leq L_{max}$ $\mathcal{T}_{L_{\min}}^{L_{\max}}(x)$: the multiset of all (L_{\min}, L_{\max}) -segmentations of x.

Example: x=0001011001{ $\{0001, 01, 10, 01\}$ } is a (2,4)-segmentation of x.

An (L_{\min}, L_{\max}) -segmentation of $x \in \Sigma^n$ is a multiset $\{\{u_0, u_1, ..., u_{m-1}\}\}$ of substrings such that: (1) $x = u_0 \circ u_1 \circ \cdots \circ u_{m-1}$. (2) $L_{min} \leq |u_i| \leq L_{max}$ for $0 \leq i < m-1$ and $|u_{m-1}| \leq L_{max}$ $\mathcal{T}_{L_{\min}}^{L_{\max}}(x)$: the multiset of all (L_{\min}, L_{\max}) -segmentations of x.

> Channel input: $x \in \Sigma^n$ Channel output: an (L_{\min}, L_{\max}) -segmentation of x.

 (L_{\min}, L_{over}) - single strand torn-paper code: code $C \subseteq \Sigma^n$ such that for any two distinct strings $x, x' \in C$, it holds that $\mathcal{T}_{L_{\min}}^{L_{\max}}(x) \cap \mathcal{T}_{L_{\min}}^{L_{\max}}(x') = \emptyset$.



Single-Strand Torn-Paper Codes: Rate

Theorem: If $L_{\min} = a \log n + O_n(1)$, for some value a > 1, then for any (L_{\min}, L_{\max}) -single-strand torn-paper code $\mathcal{C} \subseteq \Sigma^n$, $R(\mathcal{C}) \le 1 - \frac{1}{a} + o(1).$

Preliminaries: Gray Code

A *Gray Code* is an ordering of Σ^n such that any two adjacent strings differ in only one symbol position.

Example:

$$Σ = {0,1}$$
 and $n = 3$
 $|Σ^3| = 8$

0	000	4	110
1	001	5	100
2	011	6	101
3	010	7	111

Preliminaries: Index Generation

Consider:

- Index length: $I = \left[\log_q (n/L_{\min}) \right]$
- Block size: $f(n) = o(\log n)$
- $c_0, c_1, \dots, c_{q^{I}-1}$: the codewords of a *q*-ary Gray code, in order.



Preliminaries: Run-Length Limited Encoding

For t < N the set of *run-length limited (RLL)* strings is $\mathcal{RLL}_t(N) \triangleq \{x \in \Sigma^N : no t \text{-length runs of zeros}\}.$

RLL encoder: input length *m*, output length $N = N_n(m)$, and t = f(n)

$$E_m^{RLL}: \Sigma^m \to \mathcal{RLL}_{f(n)}(N_n(m)).$$

[1] M. Levy and E. Yaakobi, "Mutually uncorrelated codes for DNA storage," IEEE Trans. on Inform. Theory, vol. 65, no. 6, pp. 3671–3691, Jun. 2019. [2, Lem. 5] Y. Yehezkeally, S. Marcovich, and E. Yaakobi, "Multi-strand reconstruction from substrings," in *IEEE ITW*, 2021.

Encoder for (L_{\min}, L_{\max}) -single strand Torn-Paper code $C_A(n)$:

Input: a sequence $x \in \Sigma^{Km}$



Devide x into q^I non-overlapping substrings of length m.



Next, we encode each substring x_i into $z_i \in \Sigma^{L_{\min}}$ independently.

Encoder for (L_{\min}, L_{\max}) -single strand Torn-Paper code $C_A(n)$:

For any $0 \le i \le K - 1$: $x_i \qquad 0 \dots 0$ $\ge f(n)$ zeros

(1) Encode x_i using the RLL encoder to obtain $y_i = E_m^{RLL}(x_i)$.



(2) Let c''_i be the *i*-th encoded index and let $z_i = c''_i \circ \mathbf{10}^{f(n)} \mathbf{1} \circ y_i$.



Encoder for (L_{\min}, L_{\max}) -single strand Torn-Paper code $C_A(n)$:





Every L_{\min} -substring u of z:

- does not contain any occurrences of the marker 10001 except those explicitly added after each encoded index.
- either u contains an occurrence of the marker or it has a suffix-prefix pair whose concatenation is the marker.



Either u contains an occurrence of 1001 or it has a suffix-prefix pair whose concatenation is 1001.



 c''_i and c''_{i+1} differ only at the parity symbol and one more coordinate. c'': the concatenation of the $(\alpha - j)$ -suffix of u with the j-prefix of u.

Case 1:

$$c''_{i+1}$$
 $0 \ 1 \ 0 \ 1$
 c'' is a copy of c''_{i+1} with an erroneous parity symbol.
 Case 2:
 c''_{i+1}
 $1 \ 1 \ 1 \ 1$
 $1 \ 0 \ 0$
 c'' is equal to c''_{i} .

 c''
 $1 \ 1 \ 0 \ 1$
 $1 \ 0 \ 0$
 \uparrow
 \uparrow
 c''
 c'''
 c'''
 c'''
 c'''
 c''''
 c'''''
 c'

Hence, if the parity symbol is correct then i is the decoding of c'' and otherwise i is the decoding of c'' minus one.

Construction A – Rate

Theorem: Letting
$$f(n) \triangleq (1 + o(1))\sqrt{\log(n)}$$
 we have that
 $\operatorname{red}(\mathcal{C}_A(n)) \leq \frac{n}{a} \left(1 + \frac{2 + o(1)}{\sqrt{\log(n)}}\right)$

Hence, Construction A asymptotically meets the upper bound.



Multi-Strand Reconstruction from Substring-Composition

Reconstruction from Substring-Composition

R. Gabrys and O. Milenkovic, "Unique reconstruction of coded sequences from multiset substring spectra," *IEEE TIT*, Jun. 2019.
G. Bresler, M. Bresler, and D. Tse, "Optimal assembly for high throughput shotgun sequencing," *BMC Bioinformatics*, Jul. 2013.
H. M. Kiah, G. J. Puleo, and O. Milenkovic, "Codes for DNA sequence profiles," *IEEE TIT*, Jun. 2016.
S. Marcovich and E. Yaakobi, "Reconstruction of strings from their substrings spectrum," *IEEE TIT*, Jul. 2021.
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Notations

$$\mathcal{X}_{n,k} \triangleq \{ \mathbf{S} = \{ \{ \mathbf{x}_1, \dots, \mathbf{x}_k \} \} : \forall i, \mathbf{x}_i \in \Sigma^n \}.$$

||S||: number of unique elements in S.

- An ℓ -trace of $x \in \Sigma^n$ is a multiset of substrings such that:
- (1) All substrings are of length at least ℓ .
- (2) Succeeding substrings overlap is at least $\ell 1$.
- (3) x is covered by the substrings.

 ℓ -trace spectrum of x, denoted by $T_{\ell}(x)$: set of all ℓ -traces of x.

Example: *x*=1110111

 $\{\{11101, 1101, 10111, 0111\}\}$ is a 4-trace of x.

An ℓ -trace of $x \in \Sigma^n$ is a multiset of substrings such that: (1) All substrings are of length at least ℓ . (2) Succeeding substrings overlap is at least $\ell - 1$. (3) x is covered by the substrings.

 ℓ -trace spectrum of x, denoted by $\mathcal{T}_{\ell}(x)$: set of all ℓ -traces of x.

Example: *x*=1110111

 $\{\{11101, 1101, 10111, 0111\}\}$ is a 4-trace of x.

 $\mathcal{T}_{\ell}(S) \triangleq \bigcup_{x \in S} \mathcal{T}_{\ell}(x).$

An ℓ -trace of $x \in \Sigma^n$ is a multiset of substrings such that: (1) All substrings are of length at least ℓ . (2) Succeeding substrings overlap is at least $\ell - 1$. (3) x is covered by the substrings.

 ℓ -trace spectrum of x, denoted by $\mathcal{T}_{\ell}(x)$: set of all ℓ -traces of x.

Channel input: $S \in X_{n,k}$ Channel output: an ℓ -trace of S.

 $\mathcal{T}_{\ell}(S) \triangleq \bigcup_{x \in S} \mathcal{T}_{\ell}(x).$

Multi-strand ℓ -*trace code*: code $C \subseteq \mathcal{X}_{n,k}$ such that for any two distinct multisets $S, S' \in C$, it holds that $\mathcal{T}_{\ell}(S) \cap \mathcal{T}_{\ell}(S') = \emptyset$.



 $\mathcal{T}_{\ell}(\boldsymbol{S}')$

Preliminaries: Repeat-Free Encoding

 $\mathcal{L}_{\ell}(\mathbf{x}) \in \mathcal{T}_{\ell}(\mathbf{x})$ is the ℓ -trace that consists of all the ℓ -substrings of \mathbf{x} .

Example: x = 11101110101111 $\mathcal{L}_{12}(x) = \{\{111011101011, 110111010111, 101110101111\}\}$

For $\ell < n$ the set of ℓ -repeat-free (RF) strings is $\mathcal{RF}_{\ell}(n) \triangleq \{ \mathbf{x} \in \Sigma^{n} : no \ \ell - substring repeats \}$ $= \{ \mathbf{x} \in \Sigma^{n} : ||\mathcal{L}_{\ell}(\mathbf{x})|| = n - \ell + 1 \}.$ A multi-strand ℓ -repeat-free strings: $\mathcal{RF}_{\ell}(n,k) \triangleq \{ \mathbf{S} \in \mathcal{X}_{n,k} : ||\mathcal{L}_{\ell}(\mathbf{S})|| = k(n - \ell + 1) \}$

Preliminaries: Repeat-Free Encoding

Lemma: For all $S \in \mathcal{RF}_{\ell}(n, k)$ there exists an efficient algorithm reconstructing *S* from any ℓ -trace of *S*.

Preliminaries: Index Generation

Consider:

• Index length: $I = \left[\log_q(k) \right]$



Encoder for multi-strand ℓ -trace code C_B :



Encoder for multi-strand ℓ **-trace code** C_B **:**



For each y_i define $\widetilde{y}_i = c_i \circ y_i$



Finally, let $\operatorname{Enc}_B(\mathbf{x}) \triangleq \{\{\widetilde{\mathbf{y}}_i : i \in [k]\}\} \in \mathcal{X}_{n,k}.$

Encoder for multi-strand ℓ -trace code C_C :

Input: a sequence $x \in \Sigma^m$



Encode x using the RF encoder to obtain $y = E_{m,\ell}^{\mathcal{RF}}(x)$.



Divide y into $k \ell$ -overlapping substrings of length n.



Finally, let $\operatorname{Enc}_{\mathcal{C}}(\boldsymbol{x}) \triangleq \{\{\boldsymbol{y}_{\boldsymbol{i}}: \boldsymbol{i} \in [k]\}\} \in \mathcal{X}_{n,k}.$

Constructions B&C – Rate





Reconstruction from Substrings with Partial Overlap

Partial-Overlap Channel



Probabelistic version of this channel:

Ravi, A. N., Vahid, A., and Shomorony, I. (2022). Coded Shotgun Sequencing. ACM JSAIT, 3(1), 147-159.

An (L_{\min}, L_{over}) -trace of $x \in \Sigma^n$ is a multiset of substrings such that: (1) All substrings are of length at least L_{\min} . (2) Succeeding substrings overlap at least L_{over} . (3) x is covered by the substrings.

 (L_{\min}, L_{over}) - trace spectrum of x, denoted by $\mathcal{T}_{L_{\min}}^{L_{over}}(x)$: set of all (L_{\min}, L_{over}) -traces of x.

Example: x = 111011101011111{ $\{1110111, 1110101, 011111\}$ } is a (6,2)-trace of x.

An (L_{\min}, L_{over}) -trace of $x \in \Sigma^n$ is a multiset of substrings such that: (1) All substrings are of length at least L_{\min} . (2) Succeeding substrings overlap at least L_{over} . (3) x is covered by the substrings.

 (L_{\min}, L_{over}) - trace spectrum of x, denoted by $\mathcal{T}_{L_{\min}}^{L_{over}}(x)$: set of all (L_{\min}, L_{over}) -traces of x.

> Channel input: $x \in \Sigma^n$ Channel output: an (L_{\min}, L_{over}) -trace of x.

 (L_{\min}, L_{over}) -*trace code*: code $\mathcal{C} \subseteq \Sigma^n$ such that for any two distinct strings $x, x' \in \mathcal{C}$, it holds that $\mathcal{T}_{L_{\min}}^{L_{over}}(x) \cap \mathcal{T}_{L_{\min}}^{L_{over}}(x') = \emptyset$.





Construction for (L_{\min}, L_{over}) -Trace Codes

$$L_{\min} = a \log(n) + O_n(1), \qquad a > 1$$

$$L_{\text{over}} = \gamma L_{\min} + O_n(1), \qquad 0 < \gamma \le \frac{1}{a}$$

Preliminaries: Index Generation

Consider:

- Index length: $I \approx \left(1 \frac{1 \gamma a}{1 \gamma}\right) L_{\min}$
- Block size: $f(n) = o(\log n)$
- # blocks: $F = \frac{I}{f(n)}$



Preliminaries: Repeat-Free Encoding

For $\ell < N$ the set of *repeat-free (RF)* strings is $\mathcal{RF}_{\ell}(N) \triangleq \{ x \in \Sigma^N : no \ \ell - substring \ repeats \}.$

Lemma: For q > 2 and integers $\ell(N) > \lceil \log(N) \rceil + 3\lceil \log \log(N) \rceil$ and $\lceil \log \log(N) \rceil < t \le \left\lfloor \frac{\ell(N) - \lceil \log(N) \rceil}{3} \right\rfloor$, there exists an efficient **encoder/decoder** pair of $\mathcal{RF}_{\ell(N)}(N)$ that also does **not** contain any *t*-length runs of zeros, with rate $1 - O_n\left(\frac{t}{n} + q^{-t}\right)$.

Define encoder $E_{m,\ell}^{\mathcal{RF}}$: input length m, output length $N = N_{n,\ell}(m)$, t = f(n)

Similar result was proven in [1] for specific values of $\ell(n)$ and t

Encoder for (L_{\min}, L_{over}) -trace code C_D :

Input: a sequence $\mathbf{x} \in \Sigma^{q^{I}m}$



Devide x into q^{I} non-overlapping substrings of length m.



Next, we encode each substring x_i into $z_i \in \Sigma^{n/q^I}$ independently.

Encoder for (L_{\min}, L_{over}) -trace code C_D :

For any $0 \le i \le q^{I} - 1$ we want z_i to satisfy two properties:

(1) the index *i* can be decoded from any L_{\min} -substring of \mathbf{z}_i , and (2) the string \mathbf{z}_i can be uniquely reconstructed from any (L_{\min}, L_{over}) -trace of \mathbf{z}_i .

Then, we let

$$\operatorname{Enc}_{A}(\mathbf{x}) \triangleq \mathbf{z} = \mathbf{z}_{0} \circ \cdots \circ \mathbf{z}_{q^{I}-1}.$$

Encoder for (L_{\min}, L_{over}) -trace code C_D :



(1) Encode x_i using the RF encoder to obtain $y_i = E_{m,\ell}^{\mathcal{RF}}(x_i)$.



Encoder for (L_{\min}, L_{over}) -trace code C_D :



Encoder for (L_{\min}, L_{over}) -trace code C_D :



Lastly, we concatenate all the z_i strings, in order, to obtain the code word

 $\operatorname{Enc}_{D}(\boldsymbol{x}) \triangleq \boldsymbol{z} = \boldsymbol{z}_{0} \circ \cdots \circ \boldsymbol{z}_{q^{I}-1}.$

Construction D – Overview



Lemma: Every L_{\min} -substring \boldsymbol{u} of \boldsymbol{z} contains as subsequences at least an $(I - \mu)$ -suffix of \boldsymbol{c}_i and μ -prefix of either \boldsymbol{c}_i or \boldsymbol{c}_{i+1} for some $i \in [q^I]$ and $\mu \in [I]$, in identifiable locations.



Lemma: Every L_{\min} -substring \boldsymbol{u} of \boldsymbol{z} contains as subsequences at least an $(I - \mu)$ -suffix of \boldsymbol{c}_i and μ -prefix of either \boldsymbol{c}_i or \boldsymbol{c}_{i+1} for some $i \in [q^I]$ and $\mu \in [I]$, in identifiable locations.



Theorem : for all admissible values of *n*, the code C_D is an (L_{\min}, L_{over}) -trace code.

Proof: Take $\mathbf{z} \in \mathcal{C}_D$ and let $T \in \mathcal{T}_{L_{\min}}^{L_{\text{over}}}$ be an $(L_{\min}, L_{\text{over}})$ -trace of \mathbf{z} .



Let $\boldsymbol{u} \in T$, we can assume w.l.o.g. that $|\boldsymbol{u}| = L = L_{\min}$.

<u>Note that:</u>

- 1. The segment u does not contain any occurrences of the marker $\begin{bmatrix} 1 & 0 & 1 \end{bmatrix}$ except those explicitly added as a prefix of $z_{i,j}$ (for some i, j).
- 2. For any i, j, $|\mathbf{z}_{i,j}| \le L_{\min}$.
- 3. Either u contains an occurrence of $\begin{bmatrix} 1 & 0 & 1 \end{bmatrix}$ or it has a suffix-prefix pair whose concatenation is $\begin{bmatrix} 1 & 0 & 1 \end{bmatrix}$

Either u contains an occurrence of 1001 or it has a suffix-prefix pair whose concatenation is 1001.



We can always correctly deduce i from u.

It is therefore possible to partition T by the index i (corresponding to the substring z_i).



If u is intersecting both y_i, y_{i+1} , then u contains the complete synchronization marker 10011 hence its location in u implies the exact location of u in z.



Lemma: Every L_{over} -substring v of z contains at least ℓ consecutive symbols of $y \triangleq y_0 \circ y_1 \circ \cdots \circ y_{q^l-1}$.

Since each y_i is ℓ -repeat-free, there exist a unique way to match the overlaps of these substrings.



Lemma: Every L_{over} -substring v of z contains at least ℓ consecutive symbols of $y \triangleq y_0 \circ y_1 \circ \cdots \circ y_{q^l-1}$.

Since each y_i is ℓ -repeat-free, there exist a unique way to match the overlaps of these substrings.

Finally, once z is reconstructed we may extract $\{y_i\}_{i \in [q^I]}$, then decode $\{x_i\}_{i \in [q^I]}$ with the decoder of $E_{m,\ell}^{\mathcal{RF}}$.

Construction D – Rate

Theorem: Letting
$$f(n) \triangleq \left[\sqrt{\log(n)}\right]$$
 we have that

$$R(\mathcal{C}_D) \ge \frac{1 - \frac{1}{a}}{1 - \gamma} - \frac{\frac{1}{a}}{(\log(n))^{0.5 - \epsilon}} - O\left(\frac{1}{\sqrt{\log(n)}}\right).$$

Maximum Asymptotic Rate of (L_{\min}, L_{over}) -Trace Codes

Lemma: If $L_{\min} = a\log(n) + O_n(1)$ and $L_{over} = \gamma L_{\min} + O_n(1)$, for some a > 1 and $0 < \gamma \le \frac{1}{a}$, then any (L_{\min}, L_{over}) -trace code $C \subseteq \Sigma^n$ satisfies $R(C) \le \frac{1 - \frac{1}{a}}{1 - \gamma} + O\left(\frac{\log\log(n)}{\log(n)}\right).$

Hence, Construction D asymptotically meets the upper bound.

Corollary: If $\limsup_{n \to \infty} \frac{L_{\min}}{\log(n)} \leq 1$, then $R(\mathcal{C}) = o_n(1)$ for any (L_{\min}, L_{over}) -trace code $\mathcal{C} \subseteq \Sigma^n$.



Future Work

- Erroneous versions of the channels.
- Multistrand setup for the partial overlap channel.
- Analyze the worst-case for a more realistic setup.

References

[1] D. Bar-Lev, S. Marcovich, E. Yaakobi, and Y. Yehezkeally, "Adversarial Torn-Paper Codes", submitted to *IEEE Transactions on Information Theory*.
[2] Y. Yehezkeally, D. Bar-Lev, S. Marcovich, and E. Yaakobi, "Generalized Unique Reconstruction from Substrings", submitted to *IEEE Transactions on Information Theory*.

and also

[3] Y. Yehezkeally, S. Marcovich, and E. Yaakobi, "Multi-strand reconstruction from substrings," in *IEEE ITW*, 2021

[4] **D. Bar-Lev**, S. Marcovich, E. Yaakobi, Y. Yehezkeally, "Adversarial Torn-Paper Codes," in *IEEE ISIT*, 2022.

[5] Y. Yehezkeally, **D. Bar-Lev**, S. Marcovich, and E. Yaakobi, "Reconstruction from Substrings with Partial Overlap", in *IEEE ISITA.*, 2022.



Thank You!