Fractional Hitting Sets & SuperSampler

Efficient and Lightweight Genomic Data Sketching

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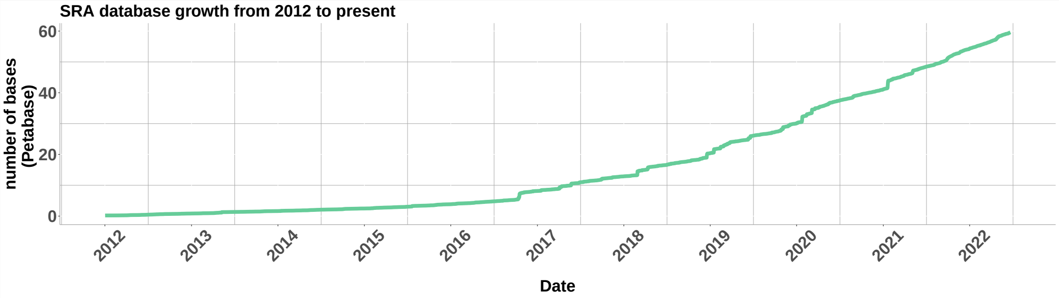
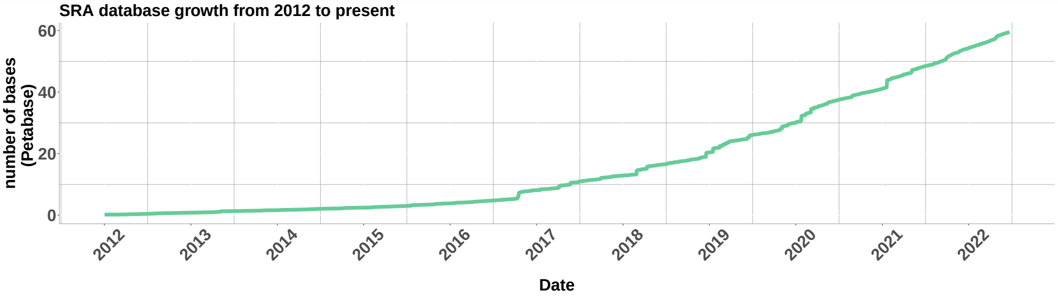

SRA database growth from 2012 to present
number of bases (Petabase)
0
20
40
60
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Date

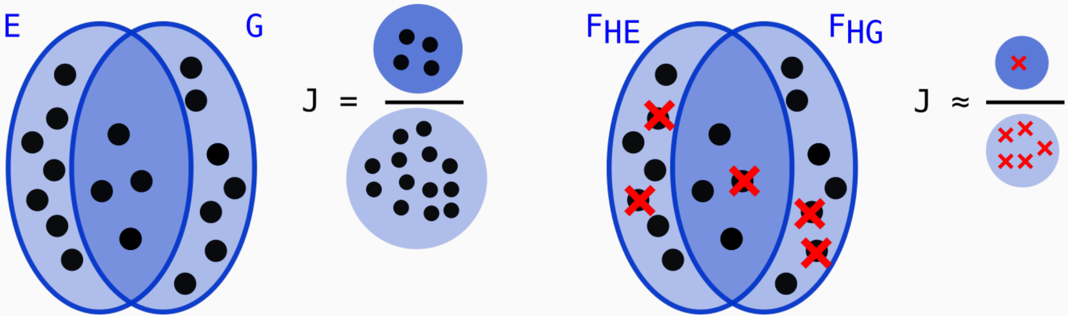


Problems

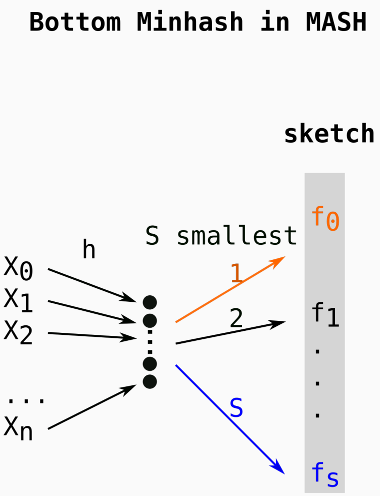
- keeps increasing
- large scale analysis not possible

Preliminaries

Jaccard index



Sketching


Bottom Minhash in MASH
sketch
S smallest
h
X0
X1
X2
...
Xn
1
2
S
f0
f1
.
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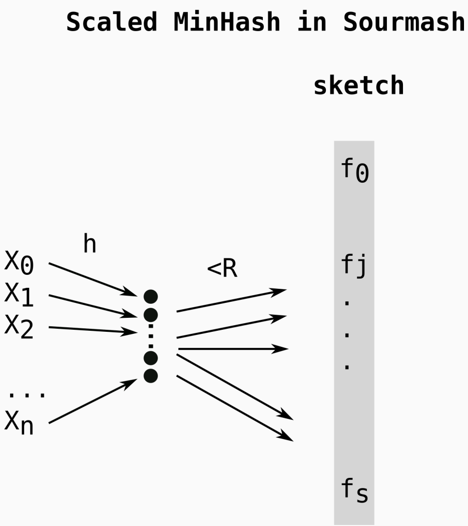
fs


Scaled MinHash in Sourmash
sketch
h
X0
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X2
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Xn
<R
f0
fj
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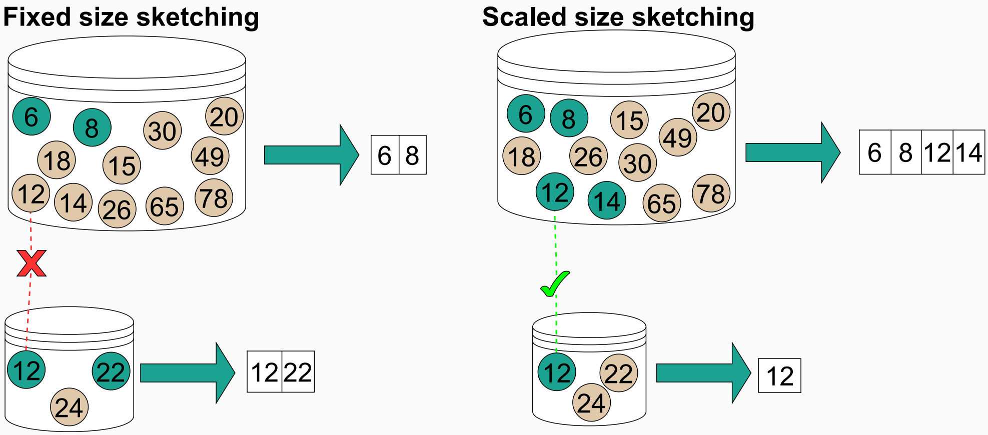
fs


Fixed size sketching
6
8
30
20
18
15
49
12
14
26
65
78
6 8
12
22
24
12 22
Scaled size sketching
6
8
15
20
49
18
26
30
12
14
65
78
6 8 12 14
12
22
24
12

Theoretical background

Minimizers & super-k-mers

Minimizer

smallest m-mer of a k-mer according to some order (e.g. lexicographical)

width parameter: $w = k - m + 1$

sequence CTGAAATGCACATTT

k-mers (k=6, m=3)

CTG**AAA**
T G**AAA**T
G**AAA**TG
AAATGC
AATGCA
ATGCAC
TGC**ACA**
GC**ACA**T
C**ACA**TT
ACATTT

super-k-mers

Minimizers & super-k-mers

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Super-k-mer

run of consecutive k-mers sharing the same minimizer

sequence CTGAAATGCACATTT

k-mers (k=6, m=3)

CTG**AAA**
T**GAAA**T
GAAATG
AAATGC
AATGCA
ATGCAC
TGC**ACA**
GC**ACA**T
C**ACA**TT
ACATTT

super-k-mers

We use minimizers as a footprint for selecting super-k-mers

We want a sparse minimizer set

Density

$$d = \frac{\#\text{selected minimizers}}{\#m\text{-mers}}$$

Density of minimizers

We want a sparse minimizer set

Density

$$d = \frac{\#\text{selected minimizers}}{\#m\text{-mers}}$$

sequence	TGTTGTGCTATT
k-mers (k=6, m=3)	T**GTT**GT
	GTT**GTG**
	TT**GTG**C
	TGT**GCT**
	GTG**CTA**
	TG**CTA**T
	GCT**ATT**
selected minimizers	.*..*.**.*

high density

(lexicographical order)

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Density

$$d = \frac{\#\text{selected minimizers}}{\#m\text{-mers}}$$

	high density (lexicographical order)	low density (TGT < CTA < ...)
sequence	TGTTGTGCTATT	TGTTGTGCTATT
k-mers (k=6, m=3)	T**GTT**GT	TGT**TGT**
	GTT**GTG**	GT**TGT**G
	TT**GTG**C	T**TGT**GC
	TGT**GCT**	**TGT**GCT
	GTG**CTA**	GTG**CTA**
	TG**CTA**T	TG**CTA**T
	GCT**ATT**	G**CTA**TT
selected minimizers	.*..*.**.*	...*....*..

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sequence	TGTTGTGCTATT
k-mers (k=6, m=3)	T**GTT**GT
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selected minimizers	.*..*.**.*

high density

(lexicographical order)

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	TGTGCT
	GTG**CTA**
	TG**CTA**T
	G**CTA**TT
selected minimizers	...*....*..

low density

(TGT < CTA < ...)

low density $\iff$ long super-k-mers

We want a sparse minimizer set

Density

$$d = \frac{\#\text{selected minimizers}}{\#m\text{-mers}}$$

Optimal density: $d = 1/w$

When using a random order, the expected density is $\frac{2}{w+1}$

	high density (lexicographical order)	low density (TGT < CTA < ...)
sequence	TGTTGTGCTATT	TGTTGTGCTATT
k-mers (k=6, m=3)	T**GTT**GT	TGT**TGT**
	GTT**GTG**	GT**TGT**G
	TT**GTG**C	T**TGT**GC
	TGT**GCT**	**TGT**GCT
	GTG**CTA**	GTG**CTA**
	TG**CTA**T	TG**CTA**T
	GCT**ATT**	G**CTA**TT
selected minimizers	.*..*.**.*	...*...*..

low density $\iff$ long super-k-mers

Universal Hitting Sets & Density lower bound

Universal Hitting Set (UHS)

set S of m-mers s.t. every run of w consecutive m-mers has $\geqslant 1$ element in S

$$1 \to 2 \to \cdots \to w-1 \to w$$

Universal Hitting Sets & Density lower bound

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Density lower bound

In any UHS, the density is $\geqslant \frac{1.5}{w+1}$ (i.e. the density factor is $\geqslant 1.5$)

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Density lower bound

In any UHS, the density is $\geqslant \frac{1.5}{w+1}$ (i.e. the density factor is $\geqslant 1.5$)

Can we cross this lower bound by relaxing some constraints?

Fractional Hitting Sets

Instead of covering every k-mer, we cover a fraction f of them

Fractional Hitting Set (FHS)

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Fractional Hitting Set (FHS)

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In practice, we select minimizers smaller than a certain threshold t

$$t = \left[1 - (1 - f)^{1/w}\right] \cdot 4^m$$

minimizers $\leqslant t$ are called small minimizers

Density upper bound

Given a covering fraction f, assuming $m > (3+\varepsilon)\log_4 w$,

$$d \leqslant \frac{2f}{w+1} + o(1/w)$$

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- $\ominus$ not very meaningful as $f \to 0$
  (since most k-mers are not covered)

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- ⊖ not very meaningful as $f \to 0$
  (since most k-mers are not covered)

Is there a more meaningful metric?

Restricted density upper bound

Given a covering fraction f, assuming $m > (3+\varepsilon)\log_4 w$,
when restricting to k-mers containing small minimizers,

$$d \leqslant 2 \cdot \frac{f + (1-f)\ln(1-f)}{f^2(w+1)} + o(1/w)$$

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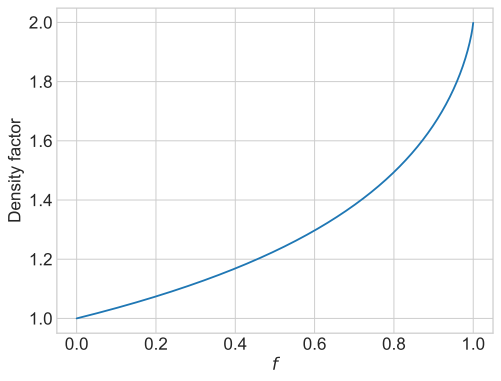
$$d \leqslant 2 \cdot \frac{f + (1-f)\ln(1-f)}{f^2(w+1)} + o(1/w)$$

- below the $\frac{1.5}{w+1}$ barrier for $f \leqslant 0.8$
- approaches optimal density as $f \to 0$



Proportion of maximal super-k-mers

The average proportion of maximal super-k-mers is

$$\left[\left(1-\frac{1}{w}\right)\frac{f}{1+f}\right]^2+\frac{1-f(1-2/w)}{1+f}$$

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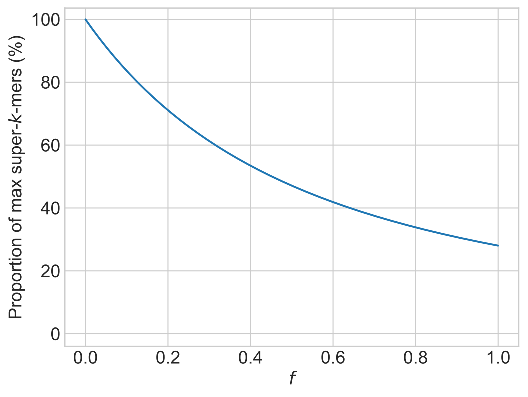
(for $w = 17$)



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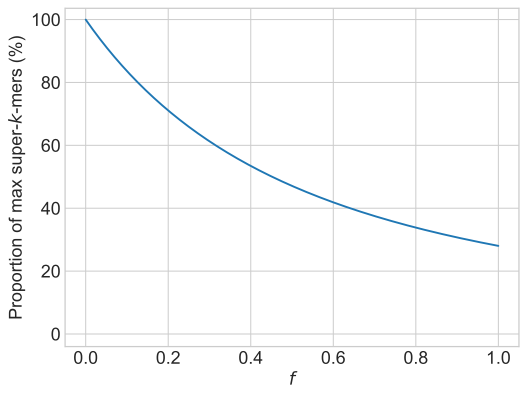
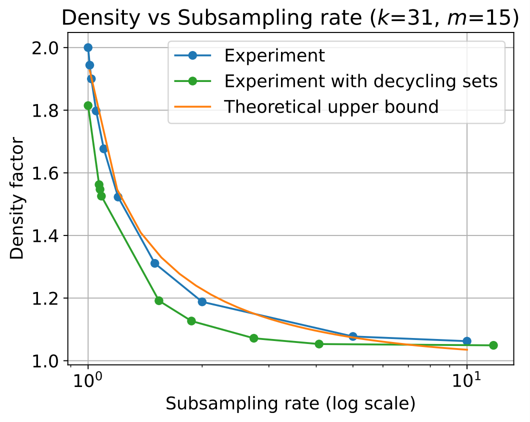
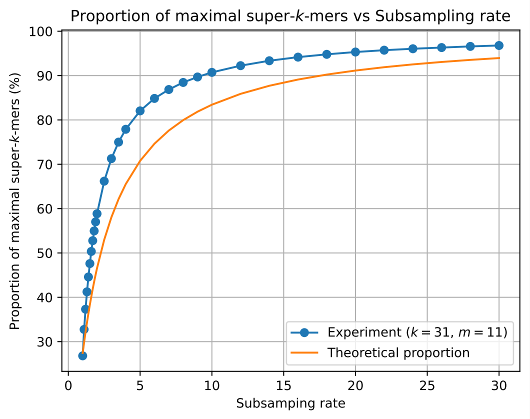


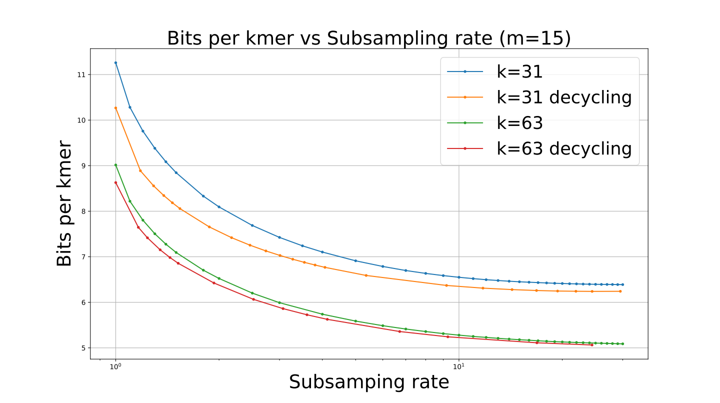
How accurate is it in practice?

Comparison with experimental results



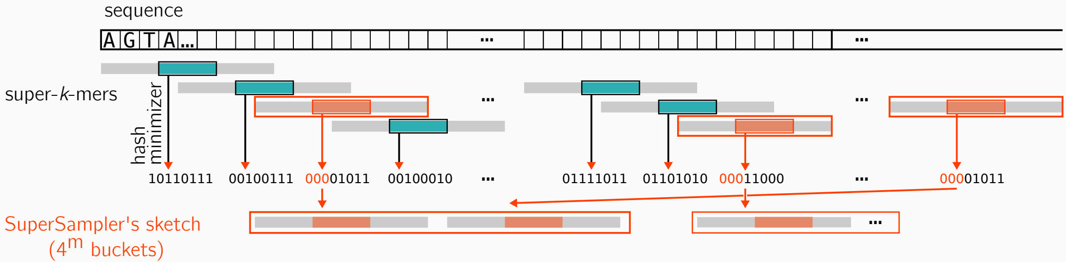


Comparison with experimental results

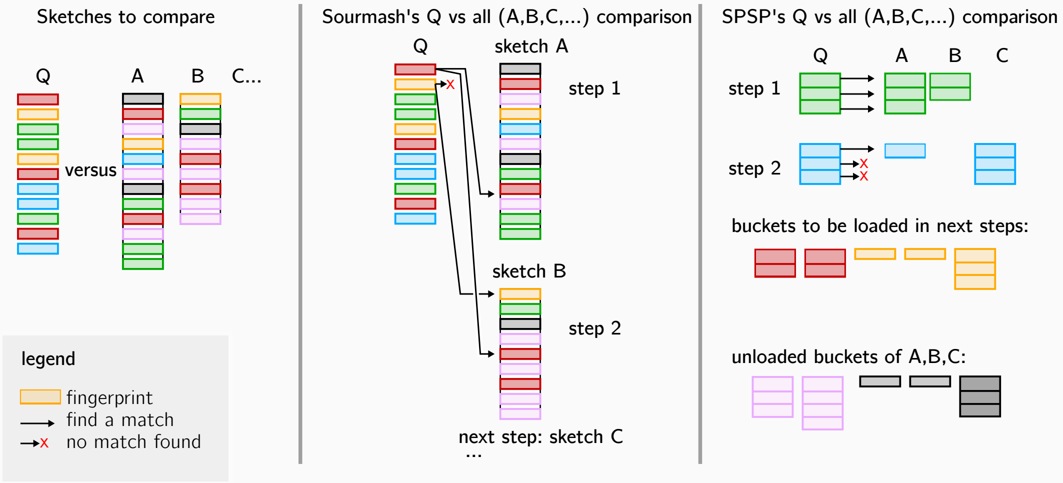


Methods

SuperSampler's sketches



Sketch comparison

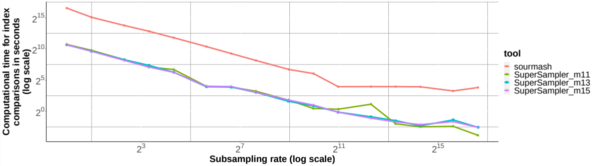


Results

Performance comparison on dissimilar data (RefSeq)

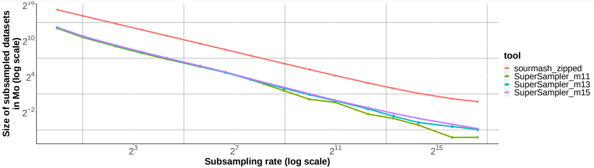
Computational time

50× faster



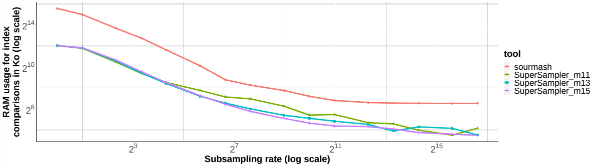
Disk usage

20× lighter



RAM usage

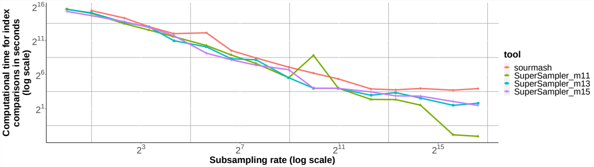
6× less RAM



Performance comparison on similar data (Salmonellas)

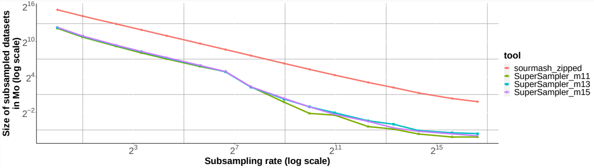
Computational time

7× faster



Disk usage

50× lighter



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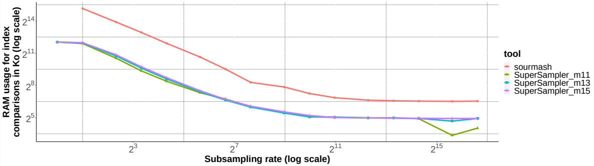

Conclusion

Take home messages

- Super-k-mers
  - robust fingerprints
  - low memory cost
- Fractional Hitting Sets
  - generalization of UHS
  - lower density
  - longer super-k-mers
  - can be combined w/ existing UHS

- Go check out our posters!
  - **Igor Martayan's poster (#123)** on the theory behind FHS
  - **My poster about SuperSampler (#147)**, if you want to have a chat with me !
- If you want to dig deeper into FHS and SuperSampler, go checkout our preprint:

Appendix

References I

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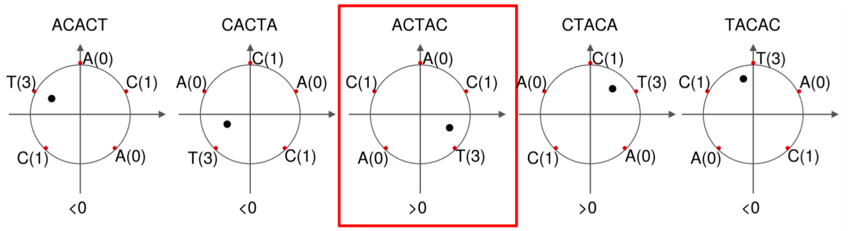
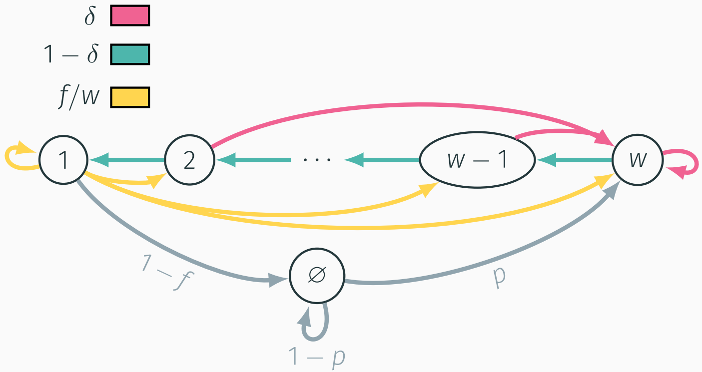
Decycling set

set S of m-mers whose removal make the De Bruijn graph acyclic

- if at least one m-mer is in S, take it in your UHS
- otherwise, use a random order to select a minimizer



Super-*k*-mers' Markov chain



- state i: small minimizer starts at i in the k-mer
- state $\varnothing$: no small minimizer in the k-mer