Vector representation of large DNA and protein strings

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The key papers to use

- Dna2vec: Consistent vector representation of variable-length k-mers, Ng,P – the one we are to discuss here;
- Distributed Representations for Biological Sequence Analysis, Kimothi et al., ;
- Continuous Distributed Representation of Biological Sequences for Deep Genomics and Deep Proteomics, Asgari, E. and Mofrad, M;

Bioinformatics 101

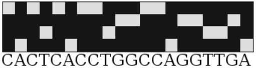
Biological data are complex!

- Direct Data Augmentation is not really applicable;
- Working with really large (1Mb and more) DNA sequences is unclear;
- Unlike basic CV, there usually are no clue about how well we can solve the problem with given training/testing data;
- A lot of experiments are low-throughput so sample sizes can be limited and the samples may overlap;

Augmentation in Computer Vision

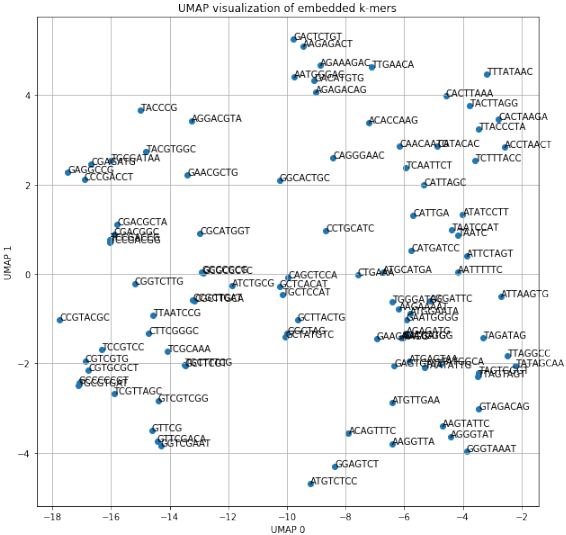
Cropped and mirrored cat pic remains a cat pic

Biological sequence case



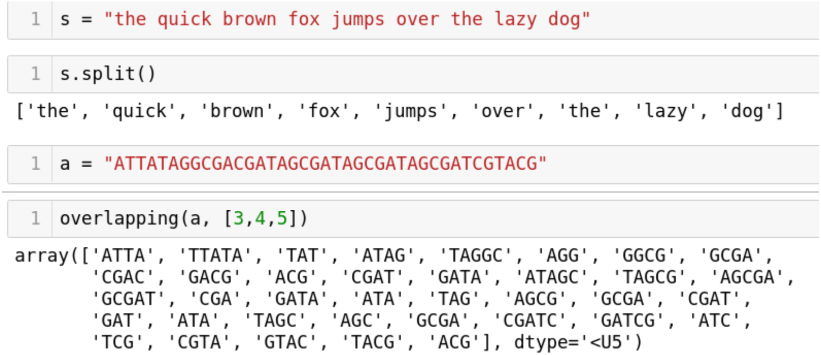
You can't say the same here

Word embeddings and their use for DNA/Proteins



Example of k-mer embedding

Problem of k-mer length choice



```
s = "the quick brown fox jumps over the lazy dog"
```

```
s.split()
```

```
['the', 'quick', 'brown', 'fox', 'jumps', 'over', 'the', 'lazy', 'dog']
```

```
a = "ATTATAGGCGACGATAGCGATAGCGATAGCGATCGTACG"
```

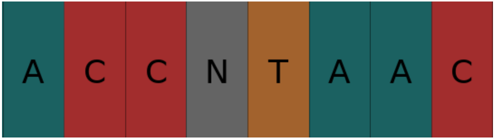
```
overlapping(a, [3,4,5])
```

```
array(['ATTA', 'TTATA', 'TAT', 'ATAG', 'TAGGC', 'AGG', 'GGCG', 'GCGA',
       'CGAC', 'GACG', 'ACG', 'CGAT', 'GATA', 'ATAGC', 'TAGCG', 'AGCGA',
       'GCGAT', 'CGA', 'GATA', 'ATA', 'TAG', 'AGCG', 'GCGA', 'CGAT',
       'GAT', 'ATA', 'TAGC', 'AGC', 'GCGA', 'CGATC', 'GATCG', 'ATC',
       'TCG', 'CGTA', 'GTAC', 'TACG', 'ACG'], dtype='<U5')
```

No words in DNA

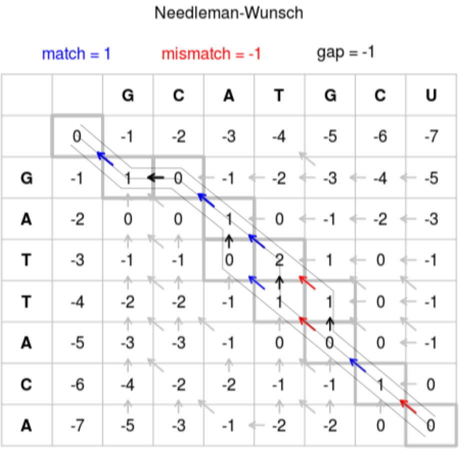
dna2vec training procedure

1. separate genome into long non-overlapping DNA fragments based on gaps;
2. convert long DNA fragments into overlapping variable-length k-mers;
3. unsupervised training of an aggregate embedding model using a two-layer neural network;
4. decompose aggregated model by k-mer lengths.



Example of gap in genome

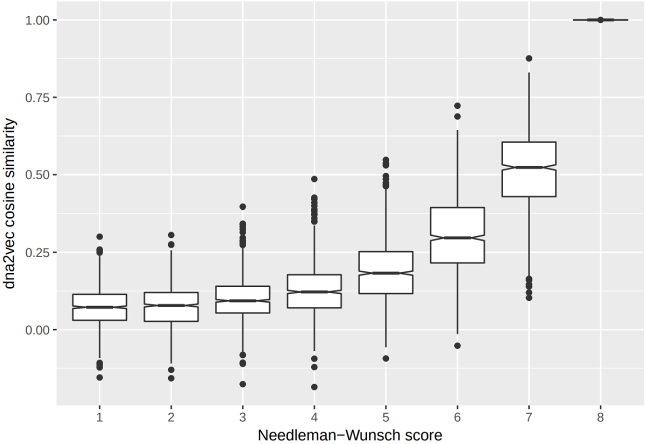
Alignment in Bioinformatics


Needleman-Wunsch
match = 1
mismatch = -1
gap = -1

		G	C	A	T	G	C	U
	0	-1	-2	-3	-4	-5	-6	-7
G	-1	1	0	-1	-2	-3	-4	-5
A	-2	0	0	1	0	-1	-2	-3
T	-3	-1	-1	0	2	1	0	-1
T	-4	-2	-2	-1	1	1	0	-1
A	-5	-3	-3	-1	0	0	0	-1
C	-6	-4	-2	-2	-1	-1	1	0
A	-7	-5	-3	-1	-2	-2	0	0

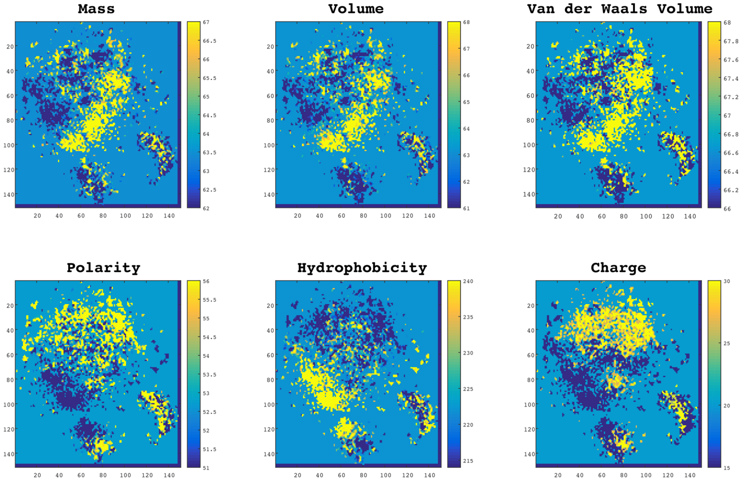
Needleman-Wunsch algorithm (Wikipedia)

Alignment similarity



Cosine similarity of dna2vec and NW score correlate with r=0.83

Possible applications



Distribution of physical properties in embedding space (Asgari and Mofrad)