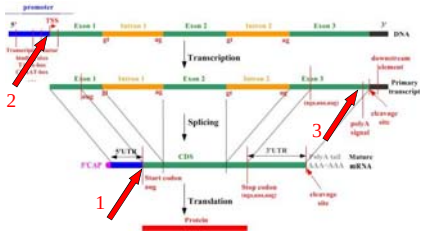
For written notes on this lecture, please read Chapters 4 and 7 of *The Practical Bioinformatician*, and Koh & Wong, "Recognition of Polyadenylation Sites from Arabidopsis Genomic Sequences", *Proc GIW 2007*, pages 73–82

CS2220: Introduction to Computational Biology

Lecture 3: Gene Feature Recognition

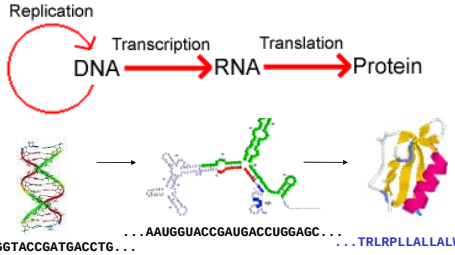
Limsoon Wong

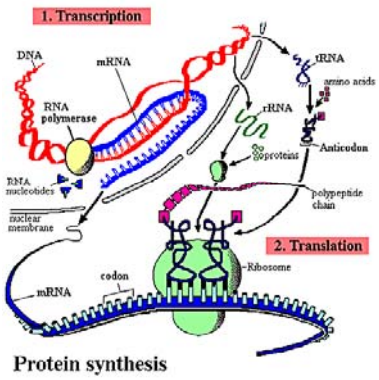
Plan



Some Relevant Biology

Central Dogma





Players in Protein Synthesis

Transcription

- **Synthesize mRNA from one strand of DNA**
  - An enzyme RNA polymerase temporarily separates double-stranded DNA
  - It begins transcription at transcription start site
  - A → A, C→C, G→G, & T→U
  - Once RNA polymerase reaches transcription stop site, transcription stops
- **Additional "steps" for Eukaryotes**
  - Transcription produces pre-mRNA that contains both introns & exons
  - 5' cap & poly-A tail are added to pre-mRNA
  - RNA splicing removes introns & mRNA is made
  - mRNA are transported out of nucleus

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Translation

- Synthesize protein from mRNA
- Each amino acid is encoded by consecutive seq of 3 nucleotides, called a codon
- The decoding table from codon to amino acid is called genetic code

- 4^3=64 diff codons
  ⇒ Codons are not 1-to-1 corr to 20 amino acids
- All organisms use the same decoding table (except some mitochrondrial genes)
- Amino acids can be classified into 4 groups. A single-base change in a codon is usu insufficient to cause a codon to code for an amino acid in diff group

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Genetic Code

- **Start codon**
  - ATG (code for M)
- **Stop codon**
  - TAA
  - TAG
  - TGA

First Position of Codon	Second Position of Codon: T	C	A	G	Third Position of Codon
T	TTT Phe [F]	TCT Ser [S]	TAT Tyr [Y]	TGT Cys [C]	T
	TTC Phe [F]	TCC Ser [S]	TAC Tyr [Y]	TGC Cys [C]	C
	TTA Leu [L]	TCA Ser [S]	TAA *Ter* [end]	TGA *Ter* [end]	A
	TTG Leu [L]	TCG Ser [S]	TAG *Ter* [end]	TGG Trp [W]	G
C	CTT Leu [L]	CCT Pro [P]	CAT His [H]	CGT Arg [R]	T
	CTC Leu [L]	CCC Pro [P]	CAC His [H]	CGC Arg [R]	C
	CTA Leu [L]	CCA Pro [P]	CAA Gln [Q]	CGA Arg [R]	A
	CTG Leu [L]	CCG Pro [P]	CAG Gln [Q]	CGG Arg [R]	G
A	ATT Ile [I]	ACT Thr [T]	AAT Asn [N]	AGT Ser [S]	T
	ATC Ile [I]	ACC Thr [T]	AAC Asn [N]	AGC Ser [S]	C
	ATA Ile [I]	ACA Thr [T]	AAA Lys [K]	AGA Arg [R]	A
	ATG Met [M]	ACG Thr [T]	AAG Lys [K]	AGG Arg [R]	G
G	GTT Val [V]	GCT Ala [A]	GAT Asp [D]	GGT Gly [G]	T
	GTC Val [V]	GCC Ala [A]	GAC Asp [D]	GGC Gly [G]	C
	GTA Val [V]	GCA Ala [A]	GAA Glu [E]	GGA Gly [G]	A
	GTG Val [V]	GCG Ala [A]	GAG Glu [E]	GGG Gly [G]	G

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Example

Example of computational translation - notice the indication of (alternative) start-codons:

```
VIRTUAL RIBOSOME
-----
Translation table: Standard SGC0

>Seq1
Reading frame: 1

  M  V  L  S  A  A  D  K  G  N  V  K  A  A  W  G  K  V  G  G  H  A  A  E  Y  G  A  E  A  L
5' ATGGTGCTGTCTGCCGCCGACAAGGGCAATGTCAAGGCCGCCTGGGGCAAGGTTGGCGGCCACGCTGCAGAGTATGGCGCAGAGGCCCTG 90
   >>>.....................................................................................

  E  R  M  F  L  S  F  P  T  T  K  T  Y  F  P  H  F  D  L  S  H  G  S  A  Q  V  K  G  H  G
5' GAGAGGATGTTCCTGAGCTTCCCCACCACCAAGACCTACTTCCCCCACTTCGACCTGAGCCACGGCTCGGCAGGTCAAGGGCCACGGC 180
   .....>>>.....................................................................................

  A  K  V  A  A  A  L  T  K  A  V  E  H  L  D  D  L  P  G  A  L  S  E  L  S  D  L  H  A  H
5' GCAAAGGTGGCCGCCGCTCTGACCAAAGCCGTGGAGCACCTGGACGACCTGCCCGGTGCCCTGTCTGAACTGAGTGACCTGCACGCTCAC 270
   ..............................>>>.....................>>>.....................>>>.....

  K  L  R  V  D  P  V  N  F  K  L  L  S  H  S  L  L  V  T  L  A  S  H  L  P  S  D  F  T  P
5' AAGCTGCGTGTGGACCCGGTCAACTTCAAGCTTCTGAGCCACTCCCTGCTGGTGACCCTGGCTCCCCACCTCCCCAGTGATTTCACCCCC 360
   .....>>>.....................>>>.....................>>>.....................>>>.....

  A  V  H  A  S  L  D  K  F  L  A  N  V  S  T  V  L  T  S  K  Y  R  *
5' GCTGTCCACGCCTCCCTGGACAAGTTCTTGGCCAACGTGAGCACCGTGCTGACCTCCAAATACCGTTAA 429
   ..............................>>>.....................>>>..........***

Annotation key:
>>> : START codon (strict)
))) : START codon (alternative)
*** : STOP
```


Recognition of Translation Initiation Sites

An introduction to the World's simplest TIS recognition system

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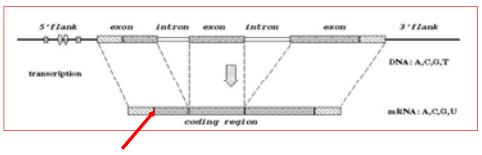
Translation Initiation Site



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A Sample cDNA

```
299 HSU27655.1 CAT U27655 Homo sapiens
CGTGTGTGCAGCAGCCTGCAGCTGCCCCAAGCCATGGCTGAACACTGACTCCCAGCTGTG      80
CCCAGGGCTTCAAAGACTTCTCAGCTTCGAGCATGGCTTTTGGCTGTCAGGGCAGCTGTA     160
GGAGGCAGATGAGAAGAGGGAGATGGCCTTGGAGGAAGGGAAGGGGCCTGGTGCCGAGGA     240
CCTCTCCTGGCCAGGAGCTTCCTCCAGGACAAGACCTTCCACCCAACAAGGACTCCCCT
.....                                                             80
.....iEEEEEEEEEEEEEEEEEEEEEEEEEEEE                               160
EEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEE     240
EEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEE
```

- **What makes the second ATG the TIS?**

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Approach

- **Training data gathering**
- **Signal generation**
  - k-grams, distance, domain know-how, ...
- **Signal selection**
  - Entropy, $\chi 2$, CFS, t-test, domain know-how...
- **Signal integration**
  - SVM, ANN, PCL, CART, C4.5, kNN, ...

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Training & Testing Data

- **Vertebrate dataset of Pedersen & Nielsen [ISMB'97]**
- **3312 sequences**
- **13503 ATG sites**
- **3312 (24.5%) are TIS**
- **10191 (75.5%) are non-TIS**
- **Use for 3-fold x-validation expts**

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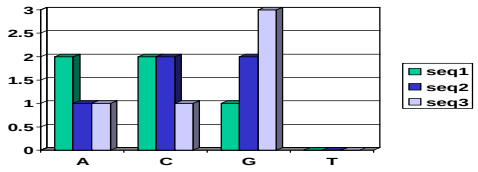
Signal Generation

- **K-grams (ie., k consecutive letters)**
  - K = 1, 2, 3, 4, 5, …
  - Window size vs. fixed position
  - Up-stream, downstream vs. any where in window
  - In-frame vs. any frame



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Signal Generation: An Example

```
299 HSU27655.1 CAT U27655 Homo sapiens
CGTGTGTGCAGCAGCCTGCAGCTGCCCCAAGCCATGGCTGAACACTGACTCCCAGCTGTG    80
CCCAGGGCTTCAAAGACTTCTCAGCTTCGAGCATGCTTTGGCTGTCAGGGCAGCTGTA   160
GGAGGCAGATGAGAAGAGGGAGATGGCCTTGGAGGAAGGGAAGGGGCCTGGTGCCGAGGA 240
CCTCTCCTGGCCAGGAGCTTCCTCCAGGACAAGACCTTCCACCCAACAAGGACTCCCCT
```

- **Window = ±100 bases**
- **In-frame, downstream**
  - GCT = 1, TTT = 1, ATG = 1…
- **Any-frame, downstream**
  - GCT = 3, TTT = 2, ATG = 2…
- **In-frame, upstream**
  - GCT = 2, TTT = 0, ATG = 0, ...

Exercise: Find the in-frame downstream ATG

Exercise: What are the possible k-grams (k=3) in this sequence?

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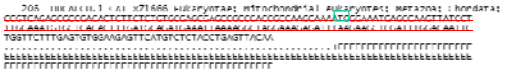
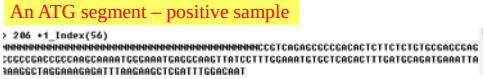
Feature Generation - Summary

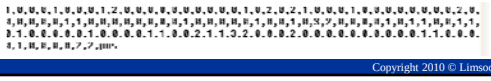
Raw Data



An ATG segment – positive sample



A feature vector --- upstream/downstream inframe 3 grams



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Too Many Features

- **For each value of k, there are 4^k * 3 * 2 k-grams**
- **If we use k = 1, 2, 3, 4, 5, we have 24 + 96 + 384 + 1536 + 6144 = 8184 features!**
- **This is too many for most machine learning algorithms**

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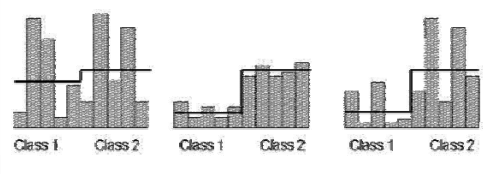
Signal Selection (Basic Idea)

- Choose a signal w/ low intra-class distance
- Choose a signal w/ high inter-class distance



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Signal Selection (e.g., t-statistics)

The t-stats of a signal is defined as

$$t = \frac{|\mu_1 - \mu_2|}{\sqrt{(\sigma_1^2/n_1) + (\sigma_2^2/n_2)}}$$

where σ_i^2 is the variance of that signal in class i, μ_i is the mean of that signal in class i, and n_i is the size of class i.

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Signal Selection (e.g., MIT-correlation)

The MIT-correlation value of a signal is defined as

$$MIT = \frac{|\mu_1 - \mu_2|}{\sigma_1 + \sigma_2}$$

where σ_i is the standard deviation of that signal in class i and μ_i is the mean of that signal in class i.

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Signal Selection (e.g., $\chi 2$)

The χ^2 value of a signal is defined as:

$$\chi^2 = \sum_{i=1}^{m} \sum_{j=1}^{k} \frac{(A_{ij} - E_{ij})^2}{E_{ij}},$$

where m is the number of intervals, k the number of classes, A_{ij} the number of samples in the ith interval, jth class, R_i the number of samples in the ith interval, C_j the number of samples in the jth class, N the total number of samples, and E_{ij} the expected frequency of A_{ij} ($E_{ij} = R_i * C_j / N$).

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Example

- Suppose you have a sample of 50 men and 50 women and the following weight distribution is observed:

	obs	exp	(obs – exp)²/exp
HM	40	60*50/100=30	3.3
HW	20	60*50/100=30	3.3
LM	10	40*50/100=20	5.0
LW	30	40*50/100=20	5.0

$\chi 2$=16.6
P = 0.00004,
df = 1
So weight and sex are not indep

- Is weight a good attribute for distinguishing men from women?

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Signal Selection (e.g., CFS)

- Instead of scoring individual signals, how about scoring a group of signals as a whole?
- CFS
  - Correlation-based Feature Selection
  - A good group contains signals that are highly correlated with the class, and yet uncorrelated with each other

Exercise: What is the main challenge in implementing CFS?

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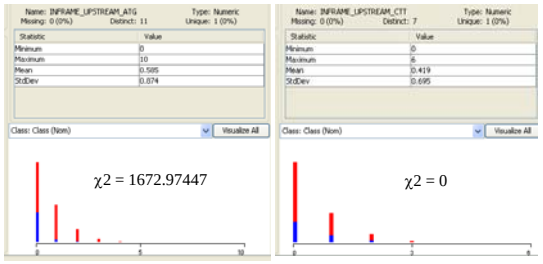
Distributions of Two Example 3-Grams



- **Which is the better one?**

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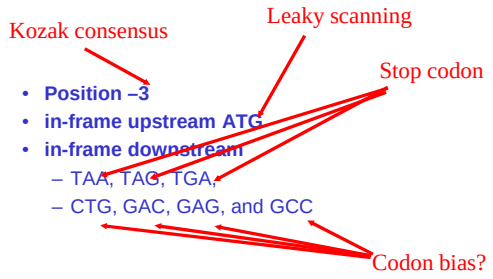
Sample k-grams Selected by CFS for Recognizing TIS



- **Position –3**
- **in-frame upstream ATG**
- **in-frame downstream**
  - TAA, TAG, TGA,
  - CTG, GAC, GAG, and GCC

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Signal Integration

- **kNN**
  - Given a test sample, find the k training samples that are most similar to it. Let the majority class win
- **SVM**
  - Given a group of training samples from two classes, determine a separating plane that maximises the margin of error
- **Naïve Bayes, ANN, C4.5, ...**

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Results (3-fold x-validation)

	predicted as positive	predicted as negative
positive	TP	FN
negative	FP	TN

Exercise: What is TP/(TP+FP)?

	TP/(TP + FN)	TN/(TN + FP)	TP/(TP + FP)	Accuracy
Naïve Bayes	84.3%	86.1%	66.3%	85.7%
SVM	73.9%	93.2%	77.9%	88.5%
Neural Network	77.6%	93.2%	78.8%	89.4%
Decision Tree	74.0%	94.4%	81.1%	89.4%

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Improvement by Voting

- **Apply any 3 of Naïve Bayes, SVM, Neural Network, & Decision Tree. Decide by majority**

	TP/(TP + FN)	TN/(TN + FP)	TP/(TP + FP)	Accuracy
NB+SVM+NN	**79.2%**	**92.1%**	**76.5%**	**88.9%**
NB+SVM+Tree	**78.8%**	**92.0%**	**76.2%**	**88.8%**
NB+NN+Tree	**77.6%**	**94.5%**	**82.1%**	**90.4%**
SVM+NN+Tree	**75.9%**	**94.3%**	**81.2%**	**89.8%**
Best of 4	**84.3%**	**94.4%**	**81.1%**	**89.4%**
Worst of 4	**73.9%**	**86.1%**	**66.3%**	**85.7%**

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Improvement by Scanning

- **Apply Naïve Bayes or SVM left-to-right until first ATG predicted as positive. That's the TIS**
- **Naïve Bayes & SVM models were trained using TIS vs. Up-stream ATG**

	TP/(TP + FN)	TN/(TN + FP)	TP/(TP + FP)	Accuracy
NB	**84.3%**	**86.1%**	**66.3%**	**85.7%**
SVM	**73.9%**	**93.2%**	**77.9%**	**88.5%**
NB+Scanning	**87.3%**	**96.1%**	**87.9%**	**93.9%**
SVM+Scanning	**88.5%**	**96.3%**	**88.6%**	**94.4%**

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Performance Comparisons

	TP/(TP + FN)	TN/(TN + FP)	TP/(TP + FP)	Accuracy
NB	84.3%	86.1%	66.3%	85.7%
Decision Tree	74.0%	94.4%	81.1%	89.4%
NB+NN+Tree	77.6%	94.5%	82.1%	90.4%
SVM+Scanning	88.5%	96.3%	88.6%	94.4%*
Pedersen&Nielsen	78%	87%	-	85%
Zien	69.9%	94.1%	-	88.1%
Hatzigeorgiou	-	-	-	94%*

* result not directly comparable

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Technique Comparisons

- **Pedersen&Nielsen [ISMB'97]**
  - Neural network
  - No explicit features
- **Zien [Bioinformatics'00]**
  - SVM+kernel engineering
  - No explicit features
- **Hatzigeorgiou [Bioinformatics'02]**
  - Multiple neural networks
  - Scanning rule
  - No explicit features
- **Our approach**
  - Explicit feature generation
  - Explicit feature selection
  - Use any machine learning method w/o any form of complicated tuning
  - Scanning rule is optional

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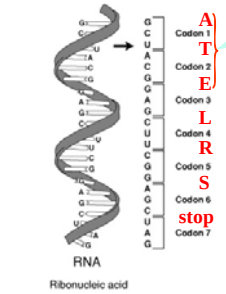
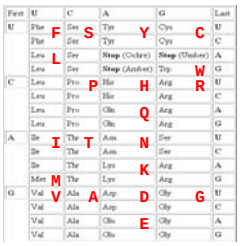
mRNA→protein



How about using k-grams from the translation?



Exercise: List the first 10 amino acid in our example sequence

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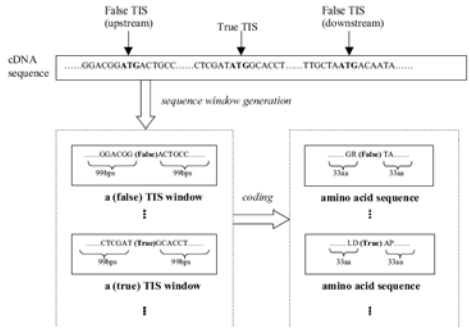
Amino-Acid Features



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Amino-Acid Features

New feature space (total of 927 features + class label)			
42 1-gram amino acid patterns	882 2-gram amino acid patterns	3 bio-know-ledge patterns	class label
UP-A, UP-R, ….,UP-N, DOWN-A, DOWN-R, …., DOWN-N (numeric type)	UP-AA, UP-AR, …., UP-NN, DOWN-AA, DOWN-AR , …., DOWN-NN (numeric type)	DOWN4-G UP3-AorG, UP-ATG (boolean type, Y or N)	True, False
Frequency as values			
1, 3, 5, 0, 4, … ⋮ 6, 5, 7, 9, 0, … ⋮	6, 2, 7, 0, 5, … ⋮ 2, 0, 3, 10, 0, … ⋮	N, N, N, ⋮ Y, Y, Y, ⋮	False ⋮ True ⋮

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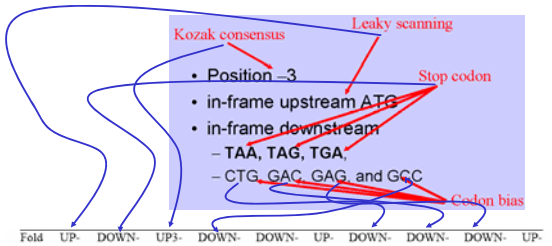
Amino Acid K-grams Discovered (by entropy)



Fold	UP-ATG	DOWN-STOP	UP3-AorG	DOWN-A	DOWN-V	UP-A	DOWN-L	DOWN-D	DOWN-E	UP-G
1	1	2	4	3	6	5	8	9	7	10
2	1	2	3	4	5	6	7	8	9	10
3	1	2	3	4	5	6	8	9	7	10

Independent Validation Sets

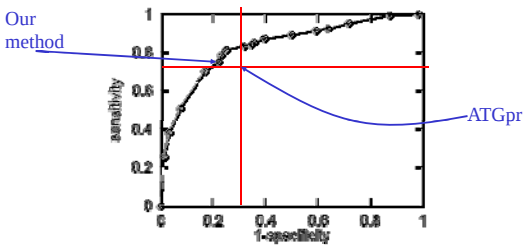
- **A. Hatzigeorgiou:**
  - 480 fully sequenced human cDNAs
  - 188 left after eliminating sequences similar to training set (Pedersen & Nielsen's)
  - 3.42% of ATGs are TIS
- **Our own:**
  - well characterized human gene sequences from chromosome X (565 TIS) and chromosome 21 (180 TIS)

Validation Results (on Hatzigeorgiou's)

Algorithm	Sensitivity	Specificity	Precision	Accuracy
SVMs(linear)	96.28%	89.15%	25.31%	89.42%
SVMs(quad)	94.14%	90.13%	26.70%	90.28%
Ensemble Trees	92.02%	92.71%	32.52%	92.68%

- Using top 100 features selected by entropy and trained on Pedersen & Nielsen's dataset

Validation Results (on Chr X and Chr 21)



- **Using top 100 features selected by entropy and trained on Pedersen & Nielsen's**

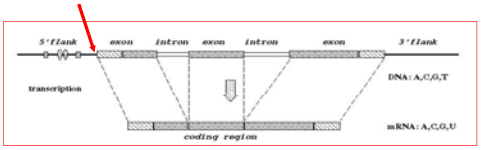
About the Inventor: Huiqing Liu

- **Huiqing Liu**
  - PhD, NUS, 2004
  - Currently Senior Scientist at Centocor
  - Asian Innovation Gold Award 2003
  - New Jersey Cancer Research Award for Scientific Excellence 2008
  - Gallo Prize 2008

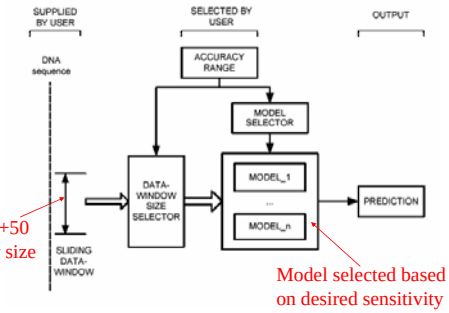
Recognition of Transcription Start Sites

An introduction to the World's best TSS recognition system:
A heavy tuning approach

Transcription Start Site



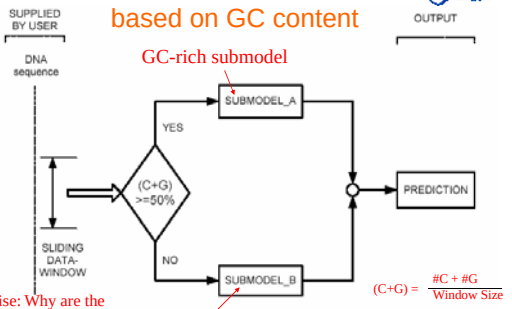
Structure of Dragon Promoter Finder



-200 to +50 window size

Model selected based on desired sensitivity

Each model has two submodels based on GC content



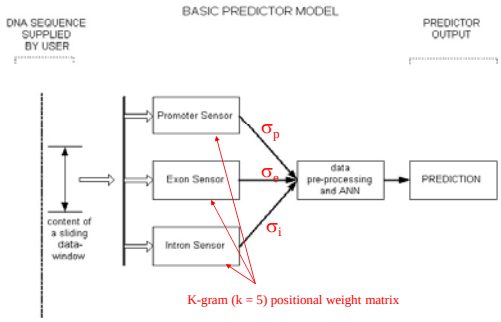
GC-rich submodel

Exercise: Why are the submodels based on GC content?

GC-poor submodel

$(C+G) = \frac{\#C + \#G}{\text{Window Size}}$

Data Analysis Within Submodel



K-gram (k = 5) positional weight matrix

Promoter, Exon, Intron Sensors

- **These sensors are positional weight matrices of k-grams, k = 5 (aka pentamers)**
- **They are calculated as below using promoter, exon, intron data respectively**

Window size

Pentamer at i^{th} position in input

$$\sigma = \frac{\left[\sum_{i=1}^{L-4} p_j^i \otimes f_{j,i}\right]}{\left[\sum_{i=1}^{L-4} \max_j f_{j,i}\right]}, \qquad p_j^i \otimes f_{j,i} = \begin{cases} f_{j,i}, \text{ if } p_i = p_j^i \\ 0, \text{ if } p_i \neq p_j^i \end{cases}$$

Frequency of jth pentamer at ith position in training window

j^{th} pentamer at i^{th} position in training window

Just to make sure you know what I mean …

- **Give me 3 DNA seq of length 10:**
  - Seq_1 = ACCGAGTTCT
  - Seq_2 = AGTGTACCTG
  - Seq_3 = AGTTCGTATG
- **Then**

1-mer	pos1	pos2	pos3	pos4	pos5	pos6	pos7	pos8	pos9	pos10
A	3/3	0/3	0/3							
C	0/3	1/3	1/3							
G	0/3	2/3	0/3							
T	0/3	0/3	2/3							

Exercise: Fill in the rest of the table

Just to make sure you know what I mean …

- **Give me 3 DNA seq of length 10:**
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  - Seq_2 = AGTGTACCTG
  - Seq_3 = AGTTCGTATG
- **Then**

Exercise: How many rows should this 2-mer table have? How many rows should the pentamer table have?

2-mer	pos1	pos2	pos3	pos4	pos5	pos6	pos7	pos8	pos9
AA	0/3	0/3	0/3						
AC	1/3	0/3	0/3						
…	…	…	…						
TT	0/3	0/3	1/3				1/3		

Exercise: Fill in the rest of the table

Data Preprocessing & ANN

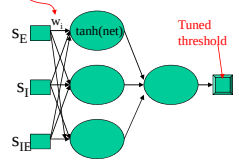
Tuning parameters

$$s_E = sat(\sigma_E, a_e, b_e),$$
$$s_I = sat(\sigma_I, a_i, b_i),$$
$$s_{EI} = sat(\sigma_e - \sigma_i, a_{ei}, b_{ei}),$$

where the function sat is defined by

$$sat(x,a,b) = \begin{cases} a, & \text{if } x > a \\ x, & \text{if } b \le x \le a. \\ b, & \text{if } b > x \end{cases}$$

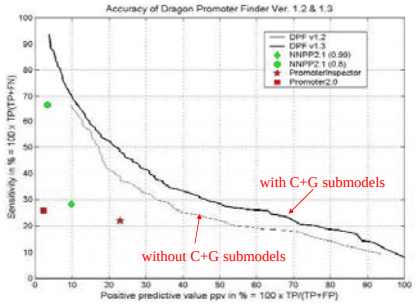
Simple feedforward ANN trained by the Bayesian regularisation method



$$\tanh(x) = \frac{e^x - e^{-x}}{e^x + e^{-x}}$$

$$net = \Sigma\, s_i * w_i$$

Accuracy Comparisons



Training Data Criteria & Preparation

- **Contain both positive and negative sequences**
- **Sufficient diversity, resembling different transcription start mechanisms**
- **Sufficient diversity, resembling different non-promoters**
- **Sanitized as much as possible**

- **TSS taken from**
  - 793 vertebrate promoters from EPD
  - -200 to +50 bp of TSS
- **non-TSS taken from**
  - GenBank,
  - 800 exons
  - 4000 introns,
  - 250 bp,
  - non-overlapping,
  - <50% identities

Tuning Data Preparation

- **To tune adjustable system parameters in Dragon, we need a separate tuning data set**

- **TSS taken from**
  - 20 full-length gene seqs with known TSS
  - -200 to +50 bp of TSS
  - no overlap with EPD
- **Non-TSS taken from**
  - 1600 human 3'UTR seqs
  - 500 human exons
  - 500 human introns
  - 250 bp
  - no overlap

Testing Data Criteria & Preparation

- **Seqs should be from the training or evaluation of other systems (no bias!)**
- **Seqs should be disjoint from training and tuning data sets**
- **Seqs should have TSS**
- **Seqs should be cleaned to remove redundancy, <50% identities**

- **159 TSS from 147 human and human virus seqs**
- **cummulative length of more than 1.15Mbp**
- **Taken from GENESCAN, GeneId, Genie, etc.**

About the Inventor: Vlad Bajic

- **Vladimir B. Bajic**
  - Principal Scientist, I²R, 2001-2006
  - Currently Director & Professor, Computational Bioscience Research Center, KAUST

Recognition of Poly-A Signal Sites

A twist to the "feature generation, feature selection, feature integration" approach

Eukaryotic Pre-mRNA Processing

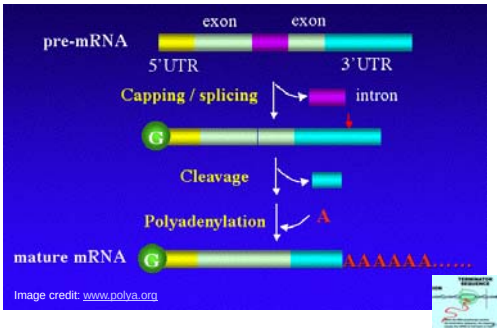


Image credit: www.polya.org

Polyadenylation in Eukaryotes

- **Addition of poly(A) tail to RNA**
  - Begins as transcription finishes
  - 3'-most segment of newly-made RNA is cleaved off
  - Poly(A) tail is then synthesized at 3' end
- **Poly(A) tail is impt for nuclear export, translation & stability of mRNA**
- **Tail is shortened over time. When short enough, the mRNA is degraded**

Source: Wikipedia

Poly-A Signals in Human (Gautheret et al., 20

Table 2. Most Significant Hexamers in 3' fragments: Clustered Hexamers

Hexamer	Observed (expected)*	% sites	P†	Position average ± SD	Location*
AAUAAA	3286 (317)	58.2	0	−16 ± 4.7	
AUUAAA	843 (112)	14.9	0	−17 ± 5.3	
AGUAAA	156 (32)	2.7	6×10^{-47}	−16 ± 5.9	
UAUAAA	180 (53)	3.2	4×10^{-43}	−18 ± 7.8	
CAUAAA	76 (23)	1.3	1×10^{-18}	−17 ± 5.9	
GAUAAA	72 (21)	1.3	2×10^{-16}	−18 ± 6.9	
AAUAUA	96 (33)	1.7	2×10^{-13}	−18 ± 6.9	
AAUACA	70 (16)	1.2	5×10^{-23}	−18 ± 8.7	
AAUAGA	43 (14)	0.7	1×10^{-9}	−18 ± 6.3	
AAAAAG	49 (11)	0.8	5×10^{-17}	−18 ± 8.9	
ACUAAA	36 (11)	0.6	1×10^{-08}	−17 ± 8.1	
AAGAAA	62 (10)	1.1	9×10^{-28}	−19 ± 11	
AAUGAA	49 (10)	0.8	4×10^{-18}	−20 ± 10	
UUUAAA	69 (20)	1.2	3×10^{-14}	−17 ± 12	
AAAACA	29 (5)	0.5	8×10^{-12}	−20 ± 10	
GGGGCU	22 (3)	0.3	9×10^{-12}	−24 ± 13	

Poly-A Signals in Arabidopsis

Table 2. Most Significant Hexamers in 3' Fragments: Clustered Hexamers

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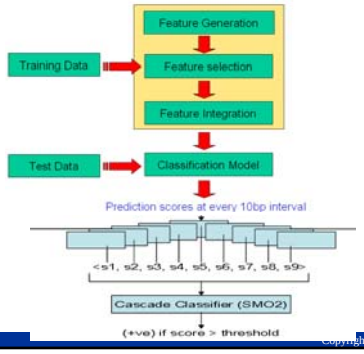
GGGGCU	22 (3)	0.3	9×10^{-12}	−24 ± 13	

In contrast to human, PAS in Arab is highly degenerate. E.g., only 10% of Arab PAS is AAUAAA!

Approach on Arab PAS Sites (I)



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Approach on Arab PAS Sites (II)

- **Data collection**
  - #1 from Hao Han, 811 +ve seq (-200/+200)
  - #2 from Hao Han, 9742 –ve seq (-200/+200)
  - #3 from Qingshun Li,
    - 6209 (+ve) seq (-300/+100)
    - 1581 (-ve) intron (-300/+100)
    - 1501 (-ve) coding (-300/+100)
    - 864 (-ve) 5'utr (-300/+100)
- **Feature generation**
  - 3-grams, compositional features (4U/1N. G/U*7, etc)
  - Freq of features above in 3 diff windows: (-110/+5), (-35/+15), (-50/+30)
- **Feature selection**
  - $\chi 2$
- **Feature integration & Cascade**
  - SVM

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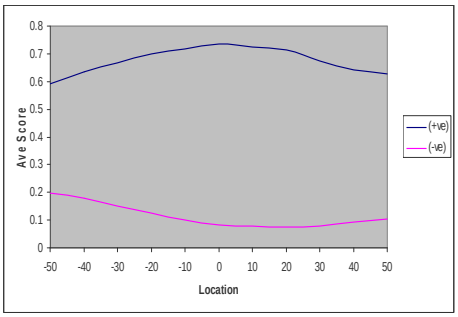
Score Profile Relative to Candidate Sites



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Validation Results

SN_0	SMO 1		SMO 2		PASS 1.0	
Control Sequences	SN & SP	Threshold	SN & SP	Threshold	SN & SP	Threshold
CDS	90%	0.26	94%	0.24	95%	3.7
5'UTR	79%	0.42	85%	0.49	78%	5.5
Intron	64%	0.59	71%	0.67	63%	6.3

Table 2. Equal-error-rate points of SMO1, SMO2, and PASS 1.0 for SN_10.

SN_10	SMO 1		SMO 2		PASS 1.0	
Control Sequences	SN & SP	Threshold	SN & SP	Threshold	SN & SP	Threshold
CDS	94%	0.36	96%	0.31	96%	4
5'UTR	86%	0.53	89%	0.6	81%	5.7
Intron	73%	0.68	77%	0.77	67%	6.6

Table 3. Equal-error-rate points of SMO1, SMO2, and PASS 1.0 for SN_30.

SN_30	SMO 1		SMO 2		PASS 1.0	
Control Sequences	SN & SP	Threshold	SN & SP	Threshold	SN & SP	Threshold
CDS	97%	0.44	97%	0.37	97%	4.3
5'UTR	90%	0.62	92%	0.67	84%	6.2
Intron	79%	0.75	83%	0.81	72%	6.8

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About the Inventor: Koh Chuan Hock

- **Koh Chuan Hock**
  - BComp (CB), NUS, 2008
  - Currently PhD candidate at SOC

Concluding Remarks…

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What have we learned?

- **Gene feature recognition applications**
  - TIS, TSS, PAS
- **General methodology**
  - "Feature generation, feature selection, feature integration"
- **Important tactics**
  - Multiple models to optimize overall performance
  - Feature transformation (DNA → amino acid)
  - Classifier cascades

Any Question?

Acknowledgements

- **The slides for PAS site prediction are adapted from slides given to me by Koh Chuan Hock**

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