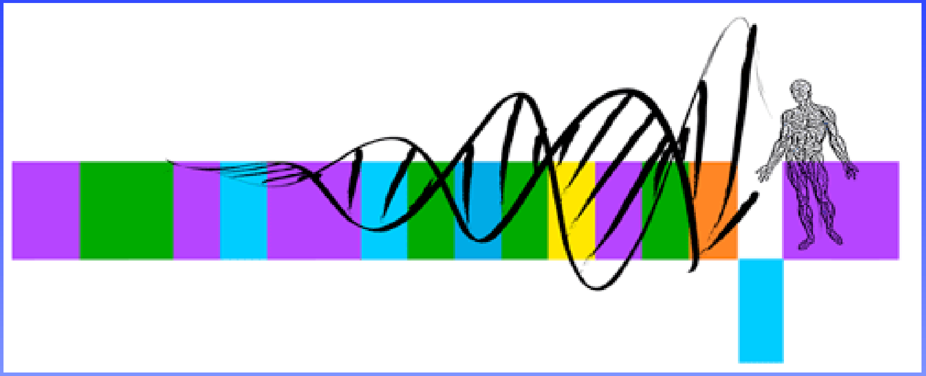

Bioinformatics for Biologists

Sequence Analysis: Part II. Pattern Searching

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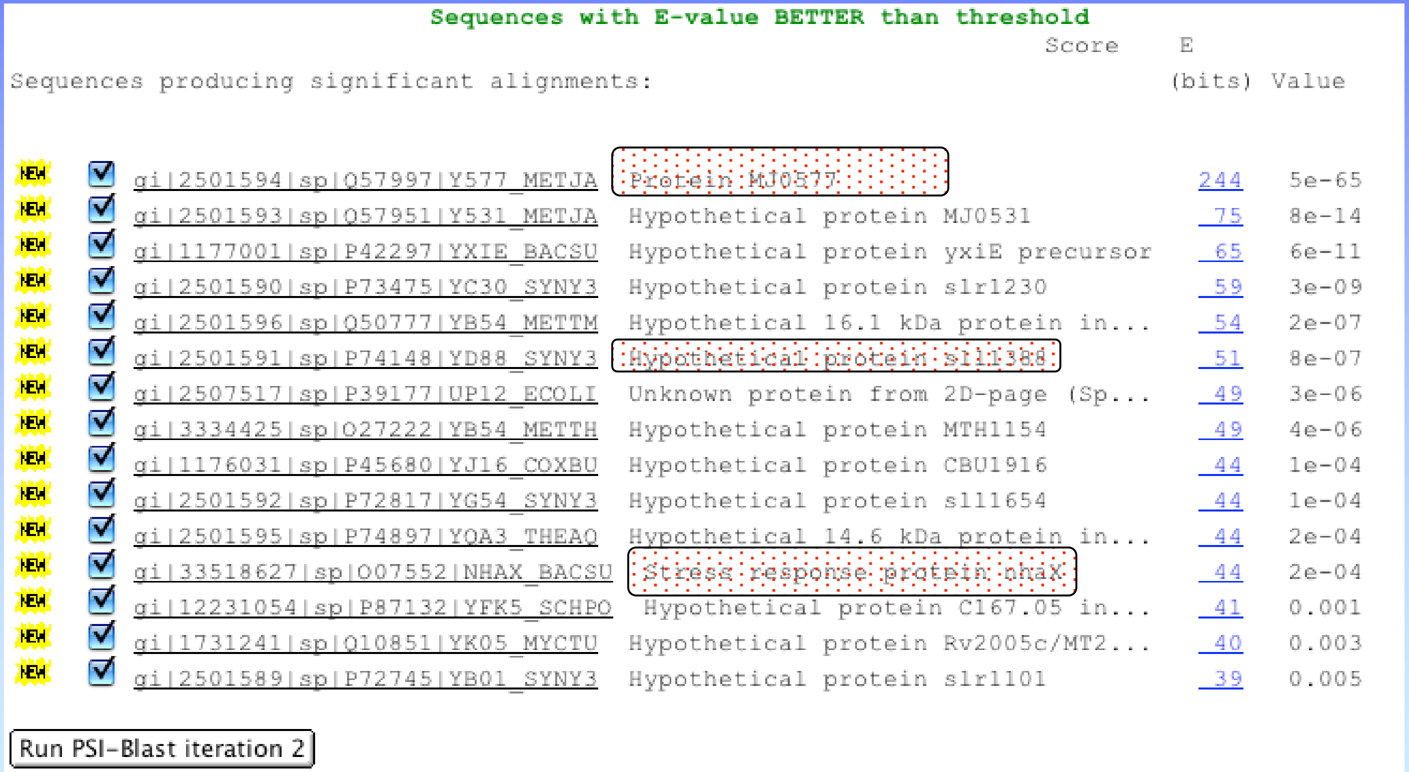
Topics to Cover

- Pattern searching
  - PSI-BLAST
  - PHI-BLAST
  - Finding patterns

PSI-BLAST

- **Position Specific Iterative** BLAST uses a profile (or position specific scoring matrix, PSSM) that is constructed (automatically) from a multiple alignment of the highest scoring hits in an initial BLAST search.
- The PSSM is generated by calculating position-specific scores for each position in the alignment. Highly conserved positions receive high scores and weakly conserved positions receive scores near zero.
- The profile is used to perform a second (etc.) BLAST search and the results of each "iteration" is used to refine the profile. This iterative searching strategy results in increased sensitivity.

Start with a BLASTP search



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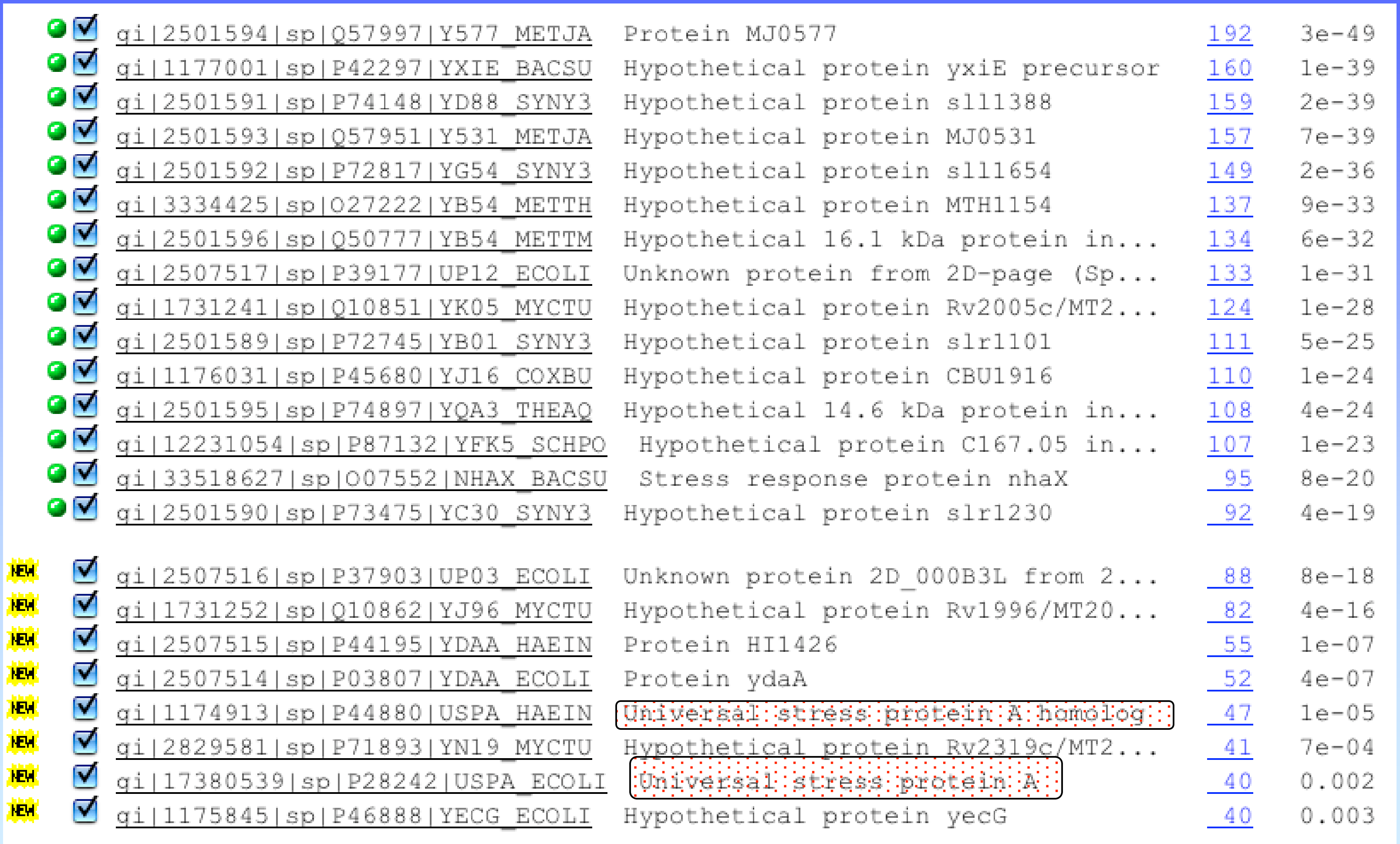
                 Sequences with E-value BETTER than threshold
                                                                    Score    E
Sequences producing significant alignments:                        (bits)  Value


NEW  ☑  gi|2501594|sp|Q57997|Y577_METJA  Protein MJ0577                       244   5e-65
NEW  ☑  gi|2501593|sp|Q57951|Y531_METJA  Hypothetical protein MJ0531           75   8e-14
NEW  ☑  gi|1177001|sp|P42297|YXIE_BACSU  Hypothetical protein yxiE precursor   65   6e-11
NEW  ☑  gi|2501590|sp|P73475|YC30_SYNY3  Hypothetical protein slr1230          59   3e-09
NEW  ☑  gi|2501596|sp|Q50777|YB54_METTM  Hypothetical 16.1 kDa protein in...   54   2e-07
NEW  ☑  gi|2501591|sp|P74148|YD88_SYNY3  Hypothetical protein sll1388          51   8e-07
NEW  ☑  gi|2507517|sp|P39177|UP12_ECOLI  Unknown protein from 2D-page (Sp...   49   3e-06
NEW  ☑  gi|3334425|sp|O27222|YB54_METTH  Hypothetical protein MTH1154          49   4e-06
NEW  ☑  gi|1176031|sp|P45680|YJ16_COXBU  Hypothetical protein CBU1916          44   1e-04
NEW  ☑  gi|2501592|sp|P72817|YG54_SYNY3  Hypothetical protein sll1654          44   1e-04
NEW  ☑  gi|2501595|sp|P74897|YQA3_THEAQ  Hypothetical 14.6 kDa protein in...   44   2e-04
NEW  ☑  gi|33518627|sp|O07552|NHAX_BACSU  Stress response protein nhaX         44   2e-04
NEW  ☑  gi|12231054|sp|P87132|YFK5_SCHPO  Hypothetical protein C167.05 in...   41   0.001
NEW  ☑  gi|1731241|sp|Q10851|YK05_MYCTU  Hypothetical protein Rv2005c/MT2...   40   0.003
NEW  ☑  gi|2501589|sp|P72745|YB01_SYNY3  Hypothetical protein slr1101          39   0.005
```

PSI-BLAST - Iteration 1



```
   ● ☑ gi|2501594|sp|Q57997|Y577_METJA  Protein MJ0577                        192  3e-49
   ● ☑ gi|1177001|sp|P42297|YXIE_BACSU  Hypothetical protein yxiE precursor  160  1e-39
   ● ☑ gi|2501591|sp|P74148|YD88_SYNY3  Hypothetical protein sll1388         159  2e-39
   ● ☑ gi|2501593|sp|Q57951|Y531_METJA  Hypothetical protein MJ0531          157  7e-39
   ● ☑ gi|2501592|sp|P72817|YG54_SYNY3  Hypothetical protein sll1654         149  2e-36
   ● ☑ gi|3334425|sp|O27222|YB54_METTH  Hypothetical protein MTH1154         137  9e-33
   ● ☑ gi|2501596|sp|Q50777|YB54_METTM  Hypothetical 16.1 kDa protein in...  134  6e-32
   ● ☑ gi|2507517|sp|P39177|UP12_ECOLI  Unknown protein from 2D-page (Sp...  133  1e-31
   ● ☑ gi|1731241|sp|Q10851|YK05_MYCTU  Hypothetical protein Rv2005c/MT2...  124  1e-28
   ● ☑ gi|2501589|sp|P72745|YB01_SYNY3  Hypothetical protein slr1101         111  5e-25
   ● ☑ gi|1176031|sp|P45680|YJ16_COXBU  Hypothetical protein CBU1916         110  1e-24
   ● ☑ gi|2501595|sp|P74897|YQA3_THEAQ  Hypothetical 14.6 kDa protein in...  108  4e-24
   ● ☑ gi|12231054|sp|P87132|YFK5_SCHPO  Hypothetical protein C167.05 in...  107  1e-23
   ● ☑ gi|33518627|sp|O07552|NHAX_BACSU  Stress response protein nhaX         95  8e-20
   ● ☑ gi|2501590|sp|P73475|YC30_SYNY3  Hypothetical protein slr1230          92  4e-19

NEW  ☑ gi|2507516|sp|P37903|UP03_ECOLI  Unknown protein 2D_000B3L from 2...   88  8e-18
NEW  ☑ gi|1731252|sp|Q10862|YJ96_MYCTU  Hypothetical protein Rv1996/MT20...   82  4e-16
NEW  ☑ gi|2507515|sp|P44195|YDAA_HAEIN  Protein HI1426                        55  1e-07
NEW  ☑ gi|2507514|sp|P03807|YDAA_ECOLI  Protein ydaA                          52  4e-07
NEW  ☑ gi|1174913|sp|P44880|USPA_HAEIN  Universal stress protein A homolog    47  1e-05
NEW  ☑ gi|2829581|sp|P71893|YN19_MYCTU  Hypothetical protein Rv2319c/MT2...   41  7e-04
NEW  ☑ gi|17380539|sp|P28242|USPA_ECOLI  Universal stress protein A           40  0.002
NEW  ☑ gi|1175845|sp|P46888|YECG_ECOLI  Hypothetical protein yecG             40  0.003
```

Amino acids

PSSM from PSI-BLAST

	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V
1	0	2	3	2	4	1	1	4	3	0	3	3	7	3	3	2	1	0	1	2
2	6	0	3	3	5	4	0	3	2	5	0	1	2	2	4	1	3	2	4	2
3	4	3	0	3	3	1	3	2	4	2	3	2	5	0	1	2	1	0	5	7
4	3	2	3	2	4	9	3	3	5	4	0	3	2	5	1	2	2	4	1	2
5	0	1	2	2	4	1	6	3	3	1	3	2	0	4	8	3	1	0	3	0
6	4	3	2	…																
•	…																			
•	…																			
N																				

POSITIONS

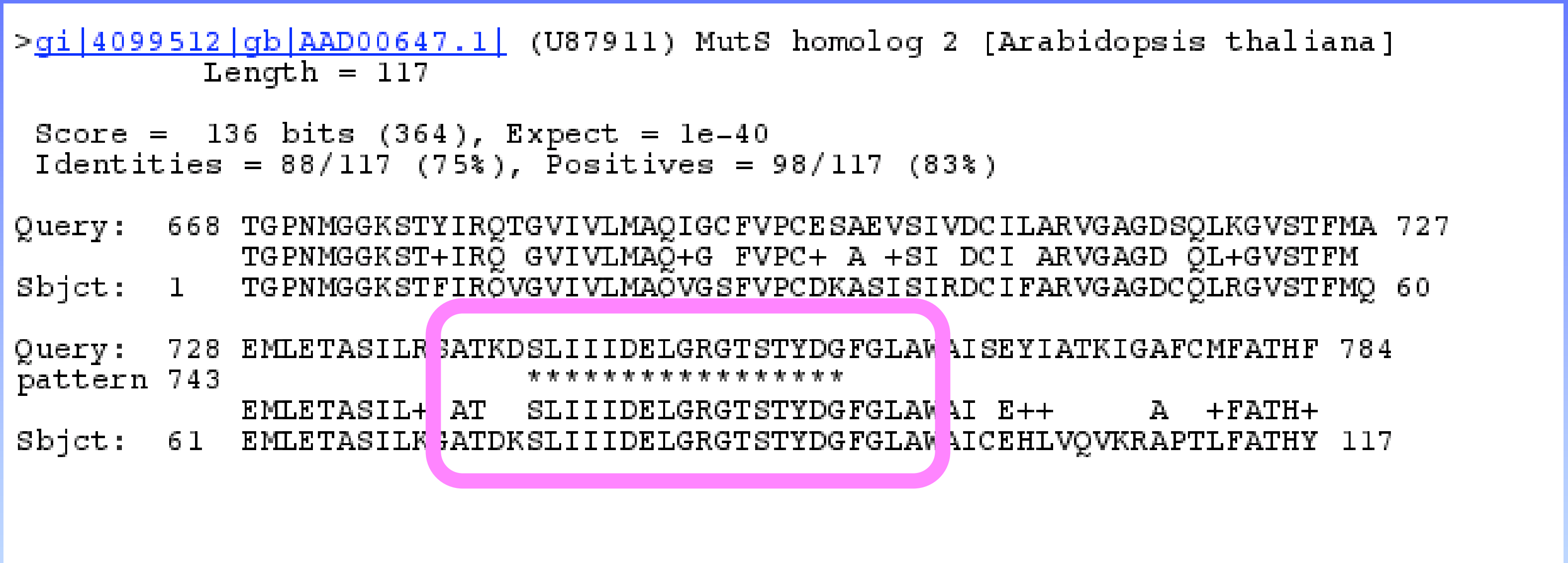
Pattern Hit Initiated (PHI)-BLAST

```
>HUMAN MSH2

MAVQPKETLQLESAAEVGFVRFFQGMPEKPTTTVRLFDRGDFYTAHGEDALLAAREVFKTQGVIKYMGPA
GAKNLQSVVLSKMNFESFVKDLLLVRQYRVEVYKNRAGNKASKENDWYLAYKASPGNLSQFEDILFGNND
MSASIGVVGVKMSAVDGQRQVGVGYVDSIQRKLGLCEFPDNDQFSNLEALLIQIGPKECVLPGGETAGDM
GKLRQIIQRGGILITERKKADFSTKDIYQDLNRLLKGKKGEQMNSAVLPEMENQVAVSSLSAVIKFLELL
SDDSNFGQFELTTFDFSQYMKLDIAAVRALNLFQGSVEDTTGSQSLAALLNKCKTPQGQRLVNQWIKQPL
MDKNRIEERLNLVEAFVEDAELRQTLQEDLLRRFPDLNRLAKKFQRQAANLQDCYRLYQGINQLPNVIQA
LEKHEGKHQKLLLAVFVTPLTDLRSDFSKFQEMIETTLDMDQVENHEFLVKPSFDPNLSELREIMNDLEK
KMQSTLISAARDLGLDPGKQIKLDSSAQFGYYFRVTCKEEKVLRNNKNFSTVDIQKNGVKFTNSKLTSLN
EEYTKNKTEYEEAQDAIVKEIVNISSGYVEPMQTLNDVLAQLDAVVSFAHVSNGAPVPYVRPAILEKGQG
RIILKASRHACVEVQDEIAFIPNDVYFEKDKQMFHIITGPNMGGKSTYIRQTGVIVLMAQIGCFVPCESA
EVSIVDCILARVGAGDSQLKGVSTFMAEMLETASILRSATKDSLIIIDELGRGTSTYDGFGLAWAISEYI
ATKIGAFCMFATHFHELTALANQIPTVNNLHVTALTTEETLTMLYQVKKGVCDQSFGIHVAELANFPKHV
                 EFQYIGESQGYDIMEPAAKKCYLEREQGEKIIQEFLSKVKQMPFTEMSEENITIKLKQ
                 VNEIISRIKVTT
```

DNA mismatch repair proteins mutS family signature

PHI-BLAST



```
>gi|4099512|gb|AAD00647.1| (U87911) MutS homolog 2 [Arabidopsis thaliana]
          Length = 117

 Score =  136 bits (364), Expect = 1e-40
 Identities = 88/117 (75%), Positives = 98/117 (83%)

Query:  668 TGPNMGGKSTYIRQTGVIVLMAQIGCFVPCESAEVSIVDCILARVGAGDSQLKGVSTFMA 727
            TGPNMGGKST+IRQ GVIVLMAQ+G FVPC+ A +SI DCI ARVGAGD QL+GVSTFM
Sbjct:  1   TGPNMGGKSTFIRQVGVIVLMAQVGSFVPCDKASISIRDCIFARVGAGDCQLRGVSTFMQ 60

Query:  728 EMLETASILRGATKDSLIIIDELGRGTSTYDGFGLAWAISEYIATKIGAFCMFATHF 784
pattern 743                ***************** 
            EMLETASIL+ AT  SLIIIDELGRGTSTYDGFGLAWAI E++     A  +FATH+
Sbjct:  61  EMLETASILKGATDKSLIIIDELGRGTSTYDGFGLAWAICEHLVQVKRAPTLFATHY 117
```

Pattern Searching

RRRRYYYY	4 purines followed by 4 pyrimidines
TATAA[1,0,0]	TATAA, allowing 1 mismatch
p1=6...8 GAGA ~p1	a hairpin with GAGA as the loop
p1=6...6 3...8 p1	exact 6 character repeat separated by up to 8
p1=6...6 3..8 p1[1,1,1]	allow one mismatch, deletion and insertion

Pattern Searching Programs

Patscan	scan_for_matches patfile < inputfile
fuzznuc, **fuzzprot,** **fuzztrans,** **dreg**	EMBOSS programs; web and Unix

Demo

- Readseq
- Entrez
- NCBI
- WU-BLAST2
- FASTA
- Smith-Waterman
- BLAT
- PatScan