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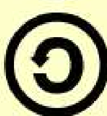

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An Introduction to Perl for Bioinformatics – Part 1

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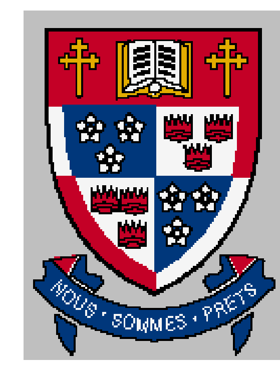


Outline

- Session 1
  - Review of the previous day
  - Perl – historical perspective
  - Expand on Regular Expression
  - General Use of Perl
  - Expand on Perl Functions and introduce Modules
  - Interactive demo on Modules
- Break
- Session 2
  - Use of Perl in Bioinformatics
  - Object Oriented Perl
  - Bioperl Overview
  - Interactive demo on Bioperl
  - Introduction to the Perl assignment

Today's Goals

- Will have become familiar with a few more advanced programming concepts
  - Regular Expression
  - Functions and Modules
  - Object Oriented Perl
- Will have heard a few common uses of Perl
- Will have learned how Perl can be used in bioinformatics
- Will have discovered Bioperl

Recap from Yesterday

- Which ones below are variables?
  – $sequence, @sequences, 74, ‘I knew this’, %seq_id, “exciting stuff”
- What are functions?
- Which part of the statement below is a function:
  – @sequences = split (/\t/, $genome);
- Other issues?

What does this program do?

```
#!/usr/bin/perl -w

#a mystery subroutine that does something
sub mystery_function{
   my ($seq1, $seq2)=@_;
   my $rDNA = reverse $seq1;
   $seq2 =~ tr/T/U/;
   my $hybrid = $rDNA.$seq2;
   return $hybrid;
}
#body of the main program
$DNA1 = “GATACAATAC”;
$DNA2 = “ATCGTAATCC”;
$answer = mystery_function($DNA1, $DNA2);
print “$answer\n”;
```

"use strict"

```
#!/usr/bin/perl -w
use strict;
#a mystery subroutine that does something
sub mystery_function{
   my ($seq1, $seq2)=@_;
   my $rDNA = reverse $seq1;
   $seq2 =~ tr/T/U/;
   my $hybrid = $rDNA.$seq2;
   return $hybrid;
}
#body of the main program
my $DNA1 = "GATACAATAC";
my $DNA2 = "ATCGTAATCC";
my $answer = mystery_function($DNA1, $DNA2);
print "$answer\n";
```

Effects of “use strict”

- Requires you to declare variables

Correct	Incorrect

`my $DNA;`
`$DNA = “ATCG”;`
or
`my $DNA = “ATCG”;`
	`$DNA = “ATCG”;`

- Warns you about possible typos in variables

No warning	Warning
`my $DNA = “ATCG”;` `$DNA =~tr/ATCG/TAGC/`	`my $DNA = “ATCG”;` `$DAN =~tr/ATCG/TAGC`

Why bother “use strict”

- Enforces some good programming rules
- Helps to prevent silly errors
- Makes trouble shooting your program easier
- Becomes essential as your code becomes longer
- We will use strict in all the code you see today and in your assignment
- **Bottom line: ALWAYS use strict**

Perl – a brief history

- Purpose: "… for scanning arbitrary text files, extracting information from those text files, and printing reports based on that information…"

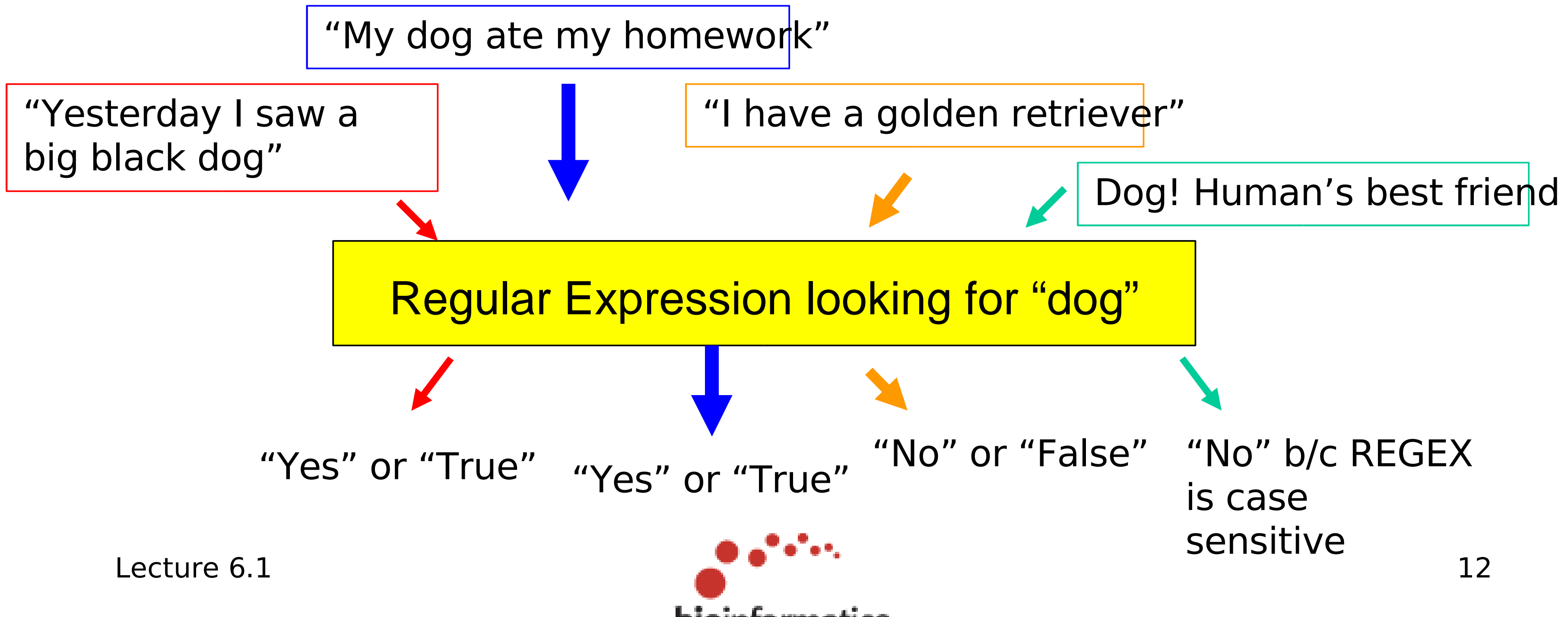
  - from perl manpage
- 1987-Perl 1.0 released
- 1993 – CPAN conceived
- 1995 – Perl 5.000 released
  - Object oriented perl
  - Modules for creating interactive web pages (CGI)
  - Modules for connection to databases (DBI)
- Current stable version of Perl is 5.8.5

How do we manipulate text?

Regular Expression

What is Regular Expression

- REGEX provides pattern matching ability
- Tells you whether a string contains a pattern or not (Note: it's a yes or no question!)



Why need Regular Expression

- Human does this quite well
- But….
- Imagine trying to find all ATG's in the human genome by hand
- Furthermore, imagine trying to find all EcoRI digestion sites (GAATTC) in the human genome

Perl REGEX example

```
my $text = “Bioinformatics Kicks Ass”;
if ($text=~/Kicks/){
  print “The text contains Kicks\n”;
}
```

- =~ is the **binding operator**
  - It says: “does the string on the left contain the pattern on the right?”
- /Kicks/ is my **pattern**
- The matching operation results in a true or false answer

More Regular Expression

- A pattern that match only one string is not very useful!
- We need symbols to represent classes of strings

- REGEX is its own little language inside Perl
  - Has different syntax and symbols!
  - Symbols which you have used in perl such as $. { } [ ] have totally different meanings in REGEX

REGEX Metacharacters

- Metacharacters allow a pattern to match different strings
  - Wildcards are examples of metacharacters
  - /.ick/ will match “kick”, “sick”, “tick”, “stick”, “kicks”, etc.
  - Perl REGEX has much more powerful metacharacters used to represent classes of characters

Types of Metacharacters

- . matches any one character or space except “\n”
- [ ] denotes a selection of characters and matches ONE of the characters in the selection.
  - What does [ATCG] match?
- \t, \s, \n match a tab, a space and a newline respectively
- \w matches any characters in [a-zA-Z0-9]
- \d matches [0-9]
- \D matches anything except [0-9]

An Example of Metacharacters

V1S 5A6?

/\w\d\D\s\d.[0-9]/

Is it a good pattern for postal code?

What else does it match?

REGEX Quantifiers

- What if you want to match a character more than once?

- What if you want to match an mRNA with a polyA tail that is at least 5 – 12 A's?

"ATG……AAAAAAAAAAAA"

REGEX Quantifiers

"ATG......AAAAAAAAAAA"

/ATG[ATCG]+A{5,12}/

- + matches one or more copies of the previous character
- * matches zero or more copies of the previous character
- ? matches zero or one copy of the previous character
- {min,max} matches a number of copies within the specified range

REGEX Anchors

- The previous pattern is not strictly correct because:
  - It'll match a string that doesn't start with ATG
  - It'll match a string that doesn't end with poly A's
- **Anchors** tell REGEX that a pattern must occur at the beginning or at the end of a string

REGEX Anchors

- ^ anchors the pattern to the start of a string
- $ anchors the pattern to the end of a string

- `/^ATG[ATCG]+A{5,12}$/`

REGEX is greedy!

- The revised pattern is still incorrect because
  - It'll match a string that has more than 12 A's at the end
- quantifiers will try to match as many copies of a sub-pattern as possible!

```
/^ATG[ATCG]+A{5,12}$/
```

"ATGGCCCGGCCTTTCCCAAAAAAAAAAAAA"

"ATGGCCCGGCCTTTCCCAAAAAAAAAAAAA"

Curb that Greed!

- ? after a quantifier prevensts REGEX from being greed
- note this is the second use of the question mark
- What is the other use of ? in REGEX?

```
/^ATG[ATCG]+?A{5,12}$/
```

"ATGGCCCGGCCTTTCCGAAAAAAAAAAAA"

"ATGGCCCGGCCTTTCCGAAAAAAAAAAAA"

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REGEX Capture

- What if you want to keep the part of a string that matches to your pattern?
- Use ( ) “memory parentheses”

“ATGGCCCGGCCTTTCCGAAAAAAAAAAAA”

```
/^ATG([ATCG]+?)A{5,12}$/
```

REGEX Capture

/^ATG([ATCG]+?)(A{5,12})$/

$1 (first group: [ATCG]+?)

$2 (second group: A{5,12})

- What's inside the first ( ) is assigned to $1
- What's inside the Second ( ) is $2 and so on
- So $2 eq "AAAAAAAAAAAA"

REGEX Modifiers

- Modifiers come after a pattern and affect the entire pattern
- You have seen //g already which does global matching (/T/g) and global replacement(s/T/U/g)
- Other useful modifiers:

//i	make pattern case insensitive
//s	let . match newline
//m	let ^ and $ (anchors) match next to embedded newline
///e	allow the replacement string to be a perl statement

REGEX Demo

- Demonstrate quantifiers
- Demonstrate anchors
- Demonstrate //i
- Demonstrate capture
- Demonstrate the effect of greedy vs. non-greedy
- Demonstrate metacharacters

Other binding operators

- =~ is called the binding operator which "binds" the a string on the left to a pattern on the right
  - E.g. $text =~/PATTERN/
- Two other binding operators: s/// and tr///
  - =~s/// (substitution) substitutes a matched pattern by a string (kind of like the "replace" function in MS Word)
  - =~tr/// (translation) translates a character to another

Summary on REGEX

- REGEX is its own little language!!!
- REGEX is used in some functions (e.g. split)
- Perl REGEX: extremely powerful and fast
- REGEX is one of the main strengths of Perl
- To learn more:
  - Learning Perl (3rd ed.) Chapters 7, 8, 9
  - Programming Perl (3rd ed.) Chapter 5
  - Mastering Regular Expression (2nd ed.)

Common Uses of Perl

- REGEX
  - Complete set of tools for pattern matching text
- System administration
  - Perl scripts can be written to automate many system administration tasks
- CGI.pm
  - Module for designing interactive web pages
- DBI.pm
  - Database Interface – allows communication between all major RDBMS systems (Oracle, MySQL, etc.)

Review on Functions

- How do we “call” a function?

```
my $sum = add (2, 3)
```

Return Value Function Name Parameter list

- Functions can take some input values (parameters) and can return some output values
- You need to assign the return values to a variable in order to use them

More Review on Functions

- Benefits of subroutines
  - Decompose a big problem into smaller, more manageable problems
  - Organize your code
  - Improve code reuse
  - Easier to test and debug your code

```
sub add {
#some code that adds numbers here
#return the sum
}
```

What are Modules

- a “logical” collection of functions
- Each collection (or module) has its own “name space”
  - Name space: a table containing the names of variables and functions used in your code

Why is name space important

Package: SEQanalysis_DNA

```
$DNA = "ATGAATACTACTAT..."

$polyAtail = "AAAAAAAAAA"

sub Revcom{}
#reverse complement sequence

sub concat{}
#concatenate two DNA sequences
```

Package: SEQanalysis_Prot

```
$exon1 = "MEDAVRSKNTMI"

$exon2 = "RSVADEGFLSMIRQH"

sub findmotif{}
#find a peptide motif

sub concat{}
#concatenate two exon
  sequences
```

SEQanalysis_DNA::concat

SEQanalysis_Prot::concat

Why Use Modules

- Modules allow you to use others' code to extend the functionality of your program
- But, use other people's modules is like going to other people's houses
  - Not everything will be the way you like it
    - Read the module documentation
  - Be nice
    - use a module as it is intended
- In Perl, each module is a file stored in some directory in your system
  - E.g. you can find cgi.pm in /usr/lib/… on your system (ask Graeme where it is)

Use Modules

- To use a module:
  - use <modulename>;
- Examples:
  - `use strict;`
  - `use Env;`
  - `use cgi qw(:standard);`
- To find out where modules are installed : `perl -V`
- To find out what standard modules are available: `perldoc perlmodlib`

Module Demo

- Demonstrate perldoc as a method to read module documentation
- Demonstrate the difference before and after using a module (use strict and use Env)
- Demonstrate the perl –V and an example of directory structure of modules

Where to find modules

- CPAN: Comprehensive Perl Archive Network
- Central repository for Perl modules and more
- "If it's written in Perl, and it's helpful and free, it's probably on CPAN"
- http://www.perl.com/CPAN/

- To install modules from CPAN
  - `perl -MCPAN -e "install 'Some::Module'"`
    - Module dependency is taken cared of automatically
    - You'll (usually) need to be root to install a module successfully
    - For details see your notes

CPAN Web Demo

- Demonstrate how to search for a module and how to access the online documentation
- We'll use Getopt::Long as an example

Interactive Demo on Getopt::Long

- Open your laptop!
- Open a terminal window
- Type `cd ~/perl_two`
- Type `emacs ./getopt_demo.pl&`
- Let's go over the example together

Summary for Session 1

- Always “use strict”
- Regular Expression is its own language inside Perl
- I encourage you to read the chapters on REGEX in Learning Perl
- A module is a logical collection of functions
- You can find module documentation by using perldoc (command line) or by going online to CPAN

Break