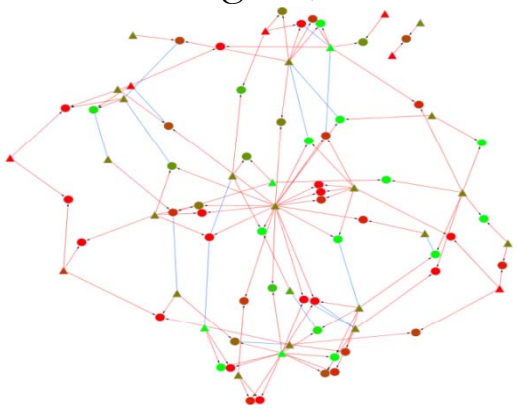
Lecture 1

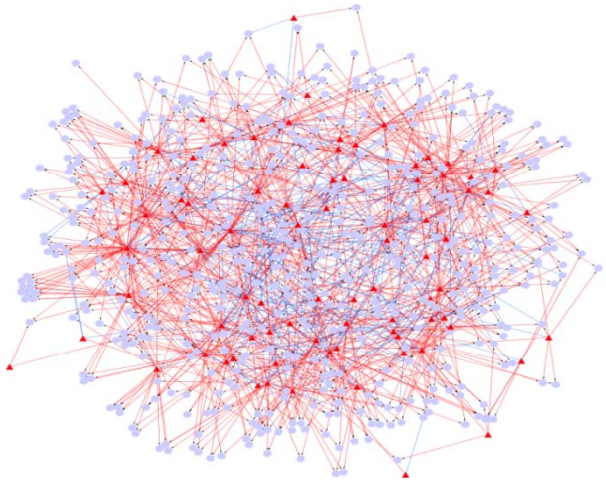
Torgeir R. Hvidsten
Assistant professor in Bioinformatics
Umeå Plant Science Center (UPSC)
Computational Life Science Centre (CLiC)

My research interests

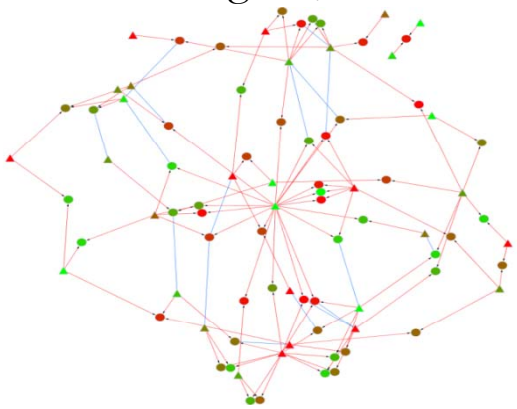
A systems biology approach to model the transcriptional network in trees

Aug. 12, 2003

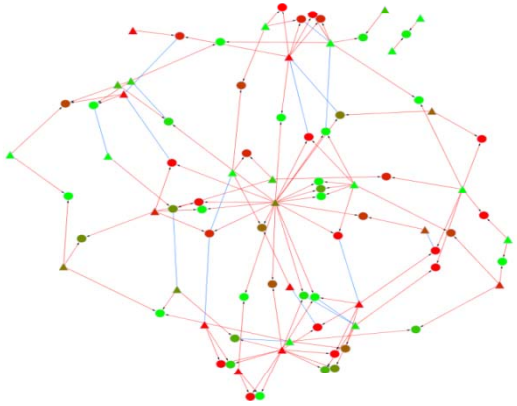




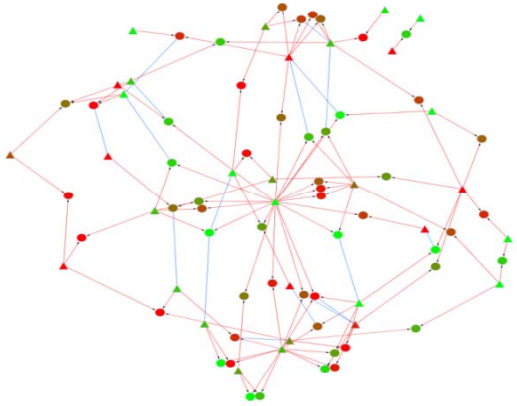
Aug. 14, 2003



Aug. 16, 2003



Aug. 17, 2003



Course goals

At the end of this course you will know how to :

- write and debug basic Perl programs
- select the correct algorithm design for a given problem and do time/space complexity analysis
- use online resources with Perl and use online Perl libraries and interfaces
- use Perl to pipeline other programs (e.g. BLAST) and parse output
- combined the above to solve practical Bioinformatics problems

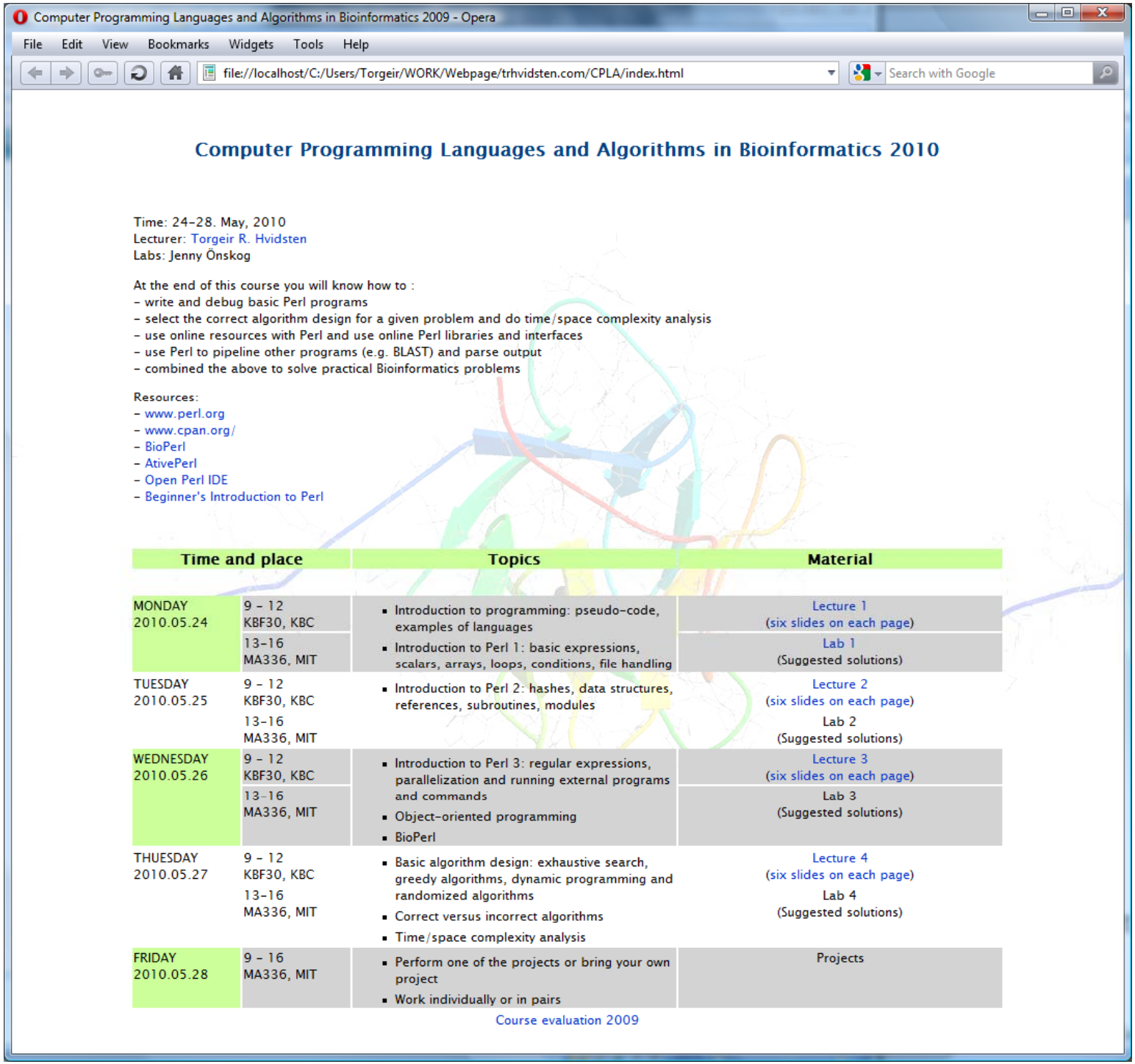
Course information (I)

- Monday - Thursday:
  - 9 – 12: lectures and lab summary
  - 13 – 16: computer labs
- Friday
  - 9 – 16: project in the computer lab
- Credit points: 2ECTS
- To pass:
  - attend lectures and labs
  - send lab and project documentation at the end of each day to: `jenny.onskog@plantphys.umu.se`

Course information (II)

- Course webpage:
  - `http://www.trhvidsten.com/CPLA/`
- Here you can find the
  - course plan
  - online resources
- and download
  - lecture slides
  - labs/project description
  - additional material

Computer labs, MA336



Computer Programming Languages and Algorithms in Bioinformatics 2010

Time: 24-28. May, 2010
Lecturer: Torgeir R. Hvidsten
Labs: Jenny Önskog

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- use online resources with Perl and use online Perl libraries and interfaces
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- combined the above to solve practical Bioinformatics problems

Resources:
- www.perl.org
- www.cpan.org/
- BioPerl
- AtivePerl
- Open Perl IDE
- Beginner's Introduction to Perl

Time and place		Topics	Material
MONDAY 2010.05.24	9 - 12 KBF30, KBC	▪ Introduction to programming: pseudo-code, examples of languages	Lecture 1 (six slides on each page)
	13-16 MA336, MIT	▪ Introduction to Perl 1: basic expressions, scalars, arrays, loops, conditions, file handling	Lab 1 (Suggested solutions)
TUESDAY 2010.05.25	9 - 12 KBF30, KBC 13-16 MA336, MIT	▪ Introduction to Perl 2: hashes, data structures, references, subroutines, modules	Lecture 2 (six slides on each page) Lab 2 (Suggested solutions)
WEDNESDAY 2010.05.26	9 - 12 KBF30, KBC	▪ Introduction to Perl 3: regular expressions, parallelization and running external programs and commands ▪ Object-oriented programming ▪ BioPerl	Lecture 3 (six slides on each page)
	13-16 MA336, MIT		Lab 3 (Suggested solutions)
THUESDAY 2010.05.27	9 - 12 KBF30, KBC 13-16 MA336, MIT	▪ Basic algorithm design: exhaustive search, greedy algorithms, dynamic programming and randomized algorithms ▪ Correct versus incorrect algorithms ▪ Time/space complexity analysis	Lecture 4 (six slides on each page) Lab 4 (Suggested solutions)
FRIDAY 2010.05.28	9 - 16 MA336, MIT	▪ Perform one of the projects or bring your own project ▪ Work individually or in pairs	Projects

Course evaluation 2009

This lecture

- Introduction to programming:
  - programming languages
  - pseudo-code
- Introduction to Perl 1
  - basic expressions
  - scalars
  - arrays
  - loops
  - conditions
  - file handling

Algorithm

- Algorithm: a sequence of instructions that one must perform in order to solve a well-formulated problem
- Correct algorithm: translate every input instance into the correct output
- Incorrect algorithm: there is at least one input instance for which the algorithm does not produce the correct output
- Many successful algorithms in bioinformatics are incorrect

Programs

- Algorithms are implemented in a programming language to form programs
- Programs consists of:
  - Variables: names with values (float, integer, string) or arrays/tables/hashes of values
  - Conditional statements: IF-THEN-ELSE
  - Loops: while, for, until, etc.
  - Modularity: procedures/functions/sub-routines/objects/methods
- Pseudo-code: programming language-independent, often used to sketch a program using pen and paper

Pseudo-code

Sorting problem: Sort a list of n integers:

$\boldsymbol{a} = (a_1, a_2, \ldots, a_n)$ e.g. $\boldsymbol{a}$ =(7,92,87,1,4,3,2,6)

SelectionSort($\boldsymbol{a}$,n)

1 **for** $i \leftarrow 1$ **to** $n-1$

2 $j \leftarrow$ Index of the smallest element among $a_i, a_{i+1}, \ldots, a_n$

3 Swap elements a_i and a_j

4 **return** $\boldsymbol{a}$

Example run

$i = 1$: (**7**,92,87,1,4,3,2,6)

$i = 2$: (1,**92**,87,7,4,3,2,6)

$i = 3$: (1,2,**87**,7,4,3,92,6)

$i = 4$: (1,2,3,**7**,4,87,92,6)

$i = 5$: (1,2,3,4,**7**,87,92,6)

$i = 6$: (1,2,3,4,6,**87**,92,7)

$i = 7$: (1,2,3,4,6,7,**92**,87)

(1,2,3,4,6,7,87,92)

Syntax versus semantics

- Syntax: the rules for constructing valid statements in a programming language
- Semantics: the meaning of a program

- A specific algorithm implemented in different programming languages would use different syntax, but have the same semantics
- Syntax is easy and can be checked before execution (the interpreter will tell you when you make syntax mistakes)
- Semantics is hard and ”bugs” typically only reveal themselves at execution time

Programming languages

- Imperative programming: describes computation as statements that change a program state (e.g. Perl, Fortran, C, and Java)
- Functional programming: treats computation as the evaluation of (mathematical) functions, and often avoids state (e.g. LISP)
- Declarative programming: while imperative programs explicitly specify an algorithm to achieve a goal, declarative programs explicitly specify the goal and leave the implementation of the algorithm to the support software (e.g. PROLOG)

Sorting: imperative/procedural

Sorting problem: Sort a list of n integers:

$\boldsymbol{a} = (a_1, a_2, \ldots, a_n)$

SelectionSort($\boldsymbol{a}$,n)

```
1    for i ← 1 to n-1
2        j ← Index of the smallest element
             among a_i, a_{i+1}, ..., a_n
3        Swap elements a_i and a_j
4    return a
```

Pseudo-code hides ugly details such as

"Swap elements a_i and a_j"

1 $tmp \leftarrow a_j$

2 $a_j \leftarrow a_i$

3 $a_i \leftarrow tmp$

or

"$j \leftarrow$ Index of the smallest element among $a_i, a_{i+1}, \ldots, a_n$"

```
IndexOfMin(array,first,last)
1       index ← first
2       for k ← first + 1 to last
3           if array_k < array_index
4               index ← k
5       return index
```

Remember, though, that the devil is in the details!

Recursion

RecursiveSelectionSort(***a***,*first*,*last*)

1 **if** (*first* < *last*)

2 *index* ← Index of the smallest element among a_{first}, $a_{first+1}$, …, a_{last}

3 Swap elements a_{first} and a_{index}

4 ***a*** ← RecursiveSelectionSort(***a***,*first*+1,*last*)

5 **return a**

Example I

Write pseudo-code for a program that solves a quadratic equation $ax^2 + bx + c = 0$:

QuadraticEquationSolver (a, b, c)

Remember that: $x = \dfrac{-b \pm \sqrt{b^2 - 4ac}}{2a}$

QuadraticEquationSolver(*a*, *b*, *c*)

1 root ← b^2-4ac;

2 **if** root < 0

3 **return** "No solution"

4 x1 ← $\frac{-b+\sqrt{root}}{2a}$

5 x2 ← $\frac{-b-\sqrt{root}}{2a}$

6 **if** x1 = x2

7 **output** "Solution: x = x1"

8 **else**

9 **output** "Solutions: x = x1 or x = x2"

Example II

Write pseudo-code for a program that removed duplicates in an array $\boldsymbol{a} = (a_1, a_2, \ldots, a_n)$

RemoveDuplicates ($\boldsymbol{a}$)

E.g. $\boldsymbol{a} = (1, 2, 2, 4, 4)$ outputs $(1, 2, 4)$

```
RemoveDuplicates(list, n)
1  newlist ← ()
2  for i ← 1 to n
3       m ←length of newlist
4       foundDuplicate ← false
5       for j ← 1 to m
6            if list_i = newlist_j
7                 foundDuplicate = true
8                 break
9       if foundDuplicate = false
10           add list_i to newlist
11 return newlist
```

Example III

Write pseudo-code for a program that counts from 0 to $\boldsymbol{n} = (n_1, n_2, ..., n_k)$:

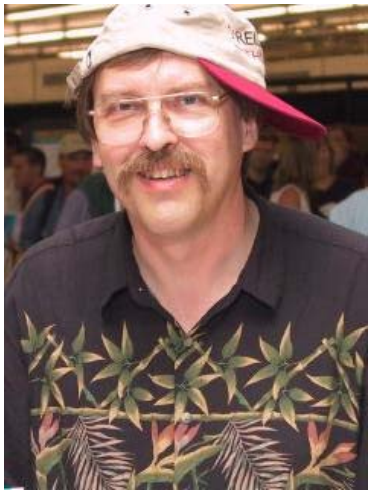
Count ($\boldsymbol{n}$)

E.g. $\boldsymbol{n} = (1, 2)$ outputs:

00
01
02
10
11
12

```
Count(n, m)
1  c ←(0, 0, …, 0)
2  while forever
3        for i ←m to 1
4           if c_i = n_i
5              c_i ←0
6           else
7              c_i ← c_i + 1
8              break
9        output c
10       if c = (0, 0, …, 0)
11          break
```

What is Perl ?



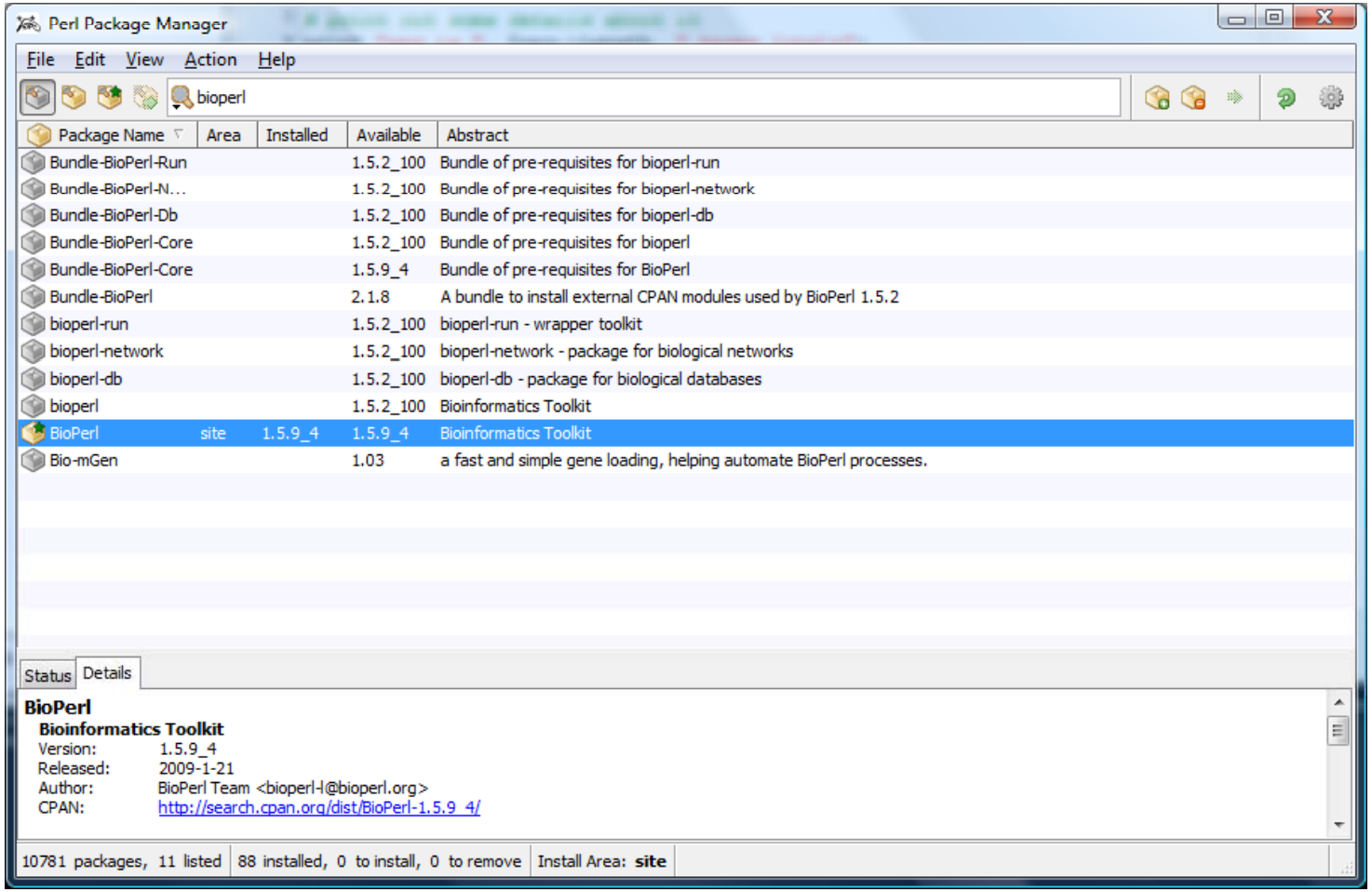
- Perl was created by Larry Wall
- Perl = Practical Extraction and Report Language
- Perl is an Open Source project
- Perl is a cross-platform programming language

Why Perl

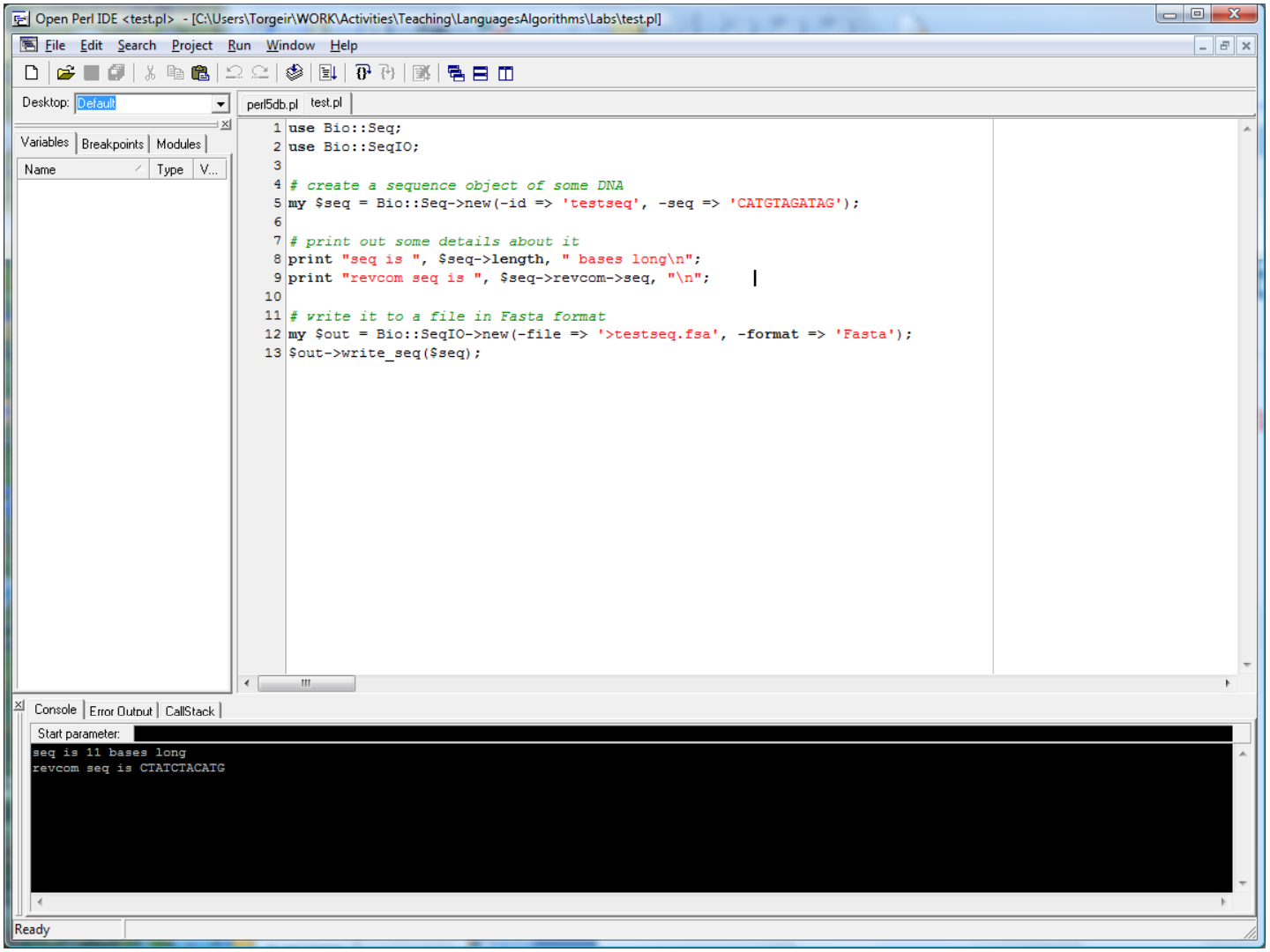
- Perl is a very popular programming language
- Perl allows a rapid development cycle
- Perl has strong text manipulation capabilities
- Perl can easily call other programs

- Existing Perl modules exists for nearly everything
  - http://www.bioperl.org
  - http://www.cpan.org/ (Comprehensive Perl Archive Network)

ActivePerl


Perl Package Manager
File Edit View Action Help
bioperl
Package Name | Area | Installed | Available | Abstract
Bundle-BioPerl-Run 1.5.2_100 Bundle of pre-requisites for bioperl-run
Bundle-BioPerl-N... 1.5.2_100 Bundle of pre-requisites for bioperl-network
Bundle-BioPerl-Db 1.5.2_100 Bundle of pre-requisites for bioperl-db
Bundle-BioPerl-Core 1.5.2_100 Bundle of pre-requisites for bioperl
Bundle-BioPerl-Core 1.5.9_4 Bundle of pre-requisites for BioPerl
Bundle-BioPerl 2.1.8 A bundle to install external CPAN modules used by BioPerl 1.5.2
bioperl-run 1.5.2_100 bioperl-run - wrapper toolkit
bioperl-network 1.5.2_100 bioperl-network - package for biological networks
bioperl-db 1.5.2_100 bioperl-db - package for biological databases
bioperl 1.5.2_100 Bioinformatics Toolkit
BioPerl site 1.5.9_4 1.5.9_4 Bioinformatics Toolkit
Bio-mGen 1.03 a fast and simple gene loading, helping automate BioPerl processes.
Status Details
BioPerl
Bioinformatics Toolkit
Version: 1.5.9_4
Released: 2009-1-21
Author: BioPerl Team <bioperl-l@bioperl.org>
CPAN: http://search.cpan.org/dist/BioPerl-1.5.9_4/
10781 packages, 11 listed 88 installed, 0 to install, 0 to remove Install Area: site

Open Perl IDE



Our first Perl program

```
use strict;
use warnings;

print "Hello world!\n";

------------------------------

Hello world!
```

“use strict" makes it harder to write bad software

”use warnings” makes Perl complain at a huge variety of things that are almost always sources of bugs in your programs

”\n” prints a new line

Perl scalars

- Perl variables that hold single values are called *Scalars*.
- Scalars hold values of many different types such as *strings, characters, floats, integers,* and *references*
- Scalars are written with a leading $, like: $sum
- Scalars, as all variables, are declared with my, like my $sum
- Perl is not a typed language: scalars can be strings, numbers, etc.

- You can reassign values of different types to a scalar:

```
my $b = 42; $b = "forty-two"; print “$b\n”;
forty-two
```

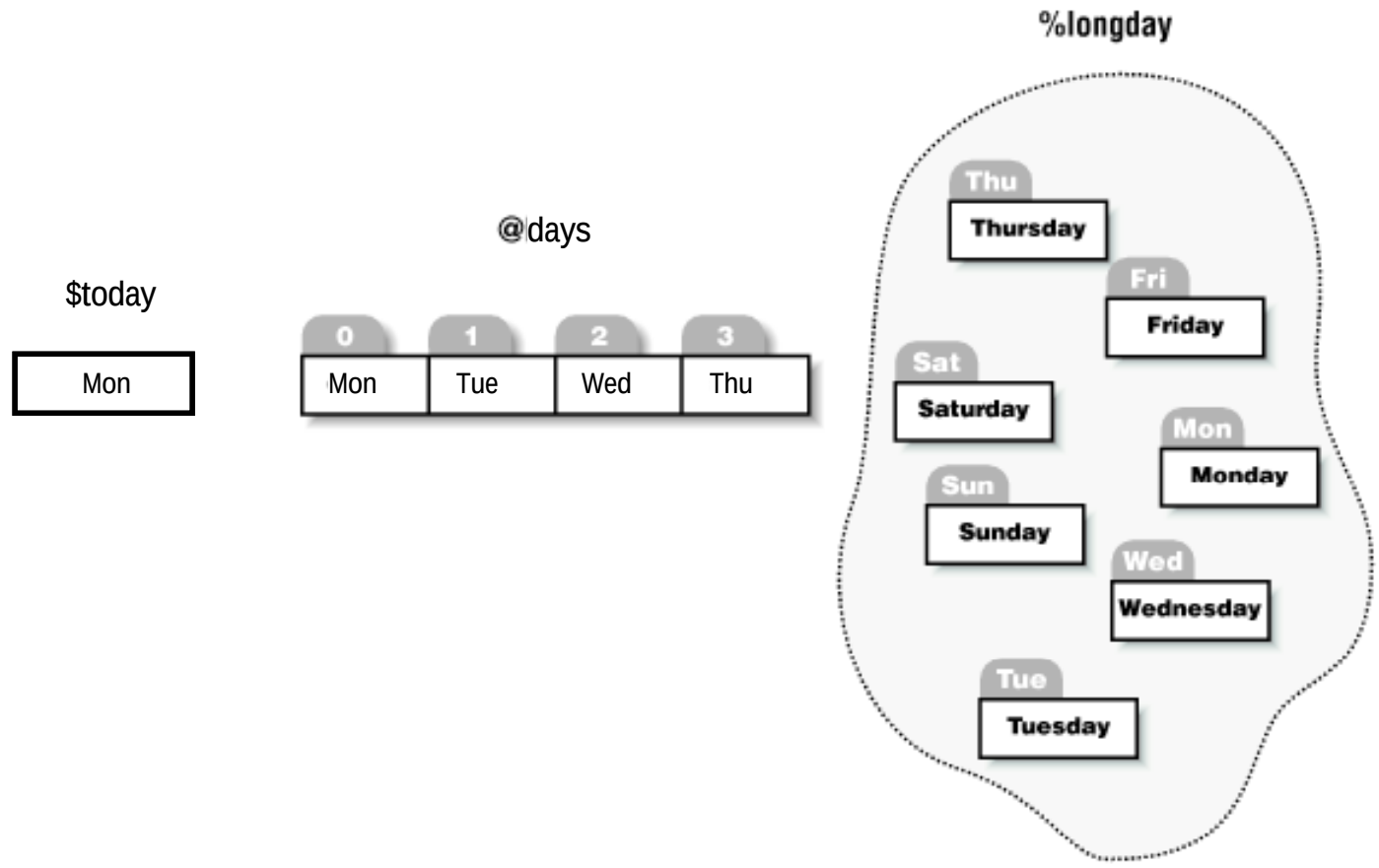
- Perl will convert between strings and numbers for you:

```
my $a = "42" + 8; print “$a\n”;
50
my $a = "Perl" + 8; print "$a\n";
Argument "Perl" isn't numeric in addition (+) at test.pl line 4.
8
```

Perl scalars: some numerical operators

- $i++; # $i = $i + 1;
- $i--; # $i = $i - 1;
- $i+= 5; # $i = $i + 5;
- $i/=5; # $i = $i / 5;
- $i**3; # $i * $i * $i;
- $i = sqrt($i)

The three fundamental datatypes in Perl



Scalar Array Hash

- The *sigills* $,@,% must always be used.
- You can use different datatypes with the same name in the same program.

Perl Arrays

- *Arrays* hold multiple ordered values.
- Arrays are written with a leading @, like: @shopping_list
- Arrays can be initialized by lists.

  my @s = ("milk","eggs","butter"); print "@s\n";

  milk eggs butter
- Arrays are indexed by integer. The first scalar in an array has index 0 and no matter its size, the last scalar has index -1:

  my @s = ("milk","eggs","butter"); print "$s[0] - $s[-1]\n";

  milk - butter
- The sizes of arrays are not declared; they grow and shrink as necessary.

  my @s = ("milk","eggs","butter"); $s[4] = "beer"; print "@s\n";

  Use of uninitialized value in join or string at test.pl line 4.

  milk eggs butter beer

Perl Arrays

- Arrays can be iterated over in foreach loops. You don't need to know their size:

```
my @s = ("milk","eggs","butter");
foreach (@s) {
    print "$_\n";
}
```

```
milk
eggs
butter
```

$_ is known as the "default input and pattern matching variable".

This is all equivalent:

```
my @s = ("milk","eggs","butter");
foreach (@s) {
    print;
    print "\n";
}
```

```
my @s = ("milk","eggs","butter");
foreach my $item (@s) {
    print "$item\n";
}
```

```
my @s = ("milk","eggs","butter");
foreach (@s) {
    print "$_\n";
}
```

Perl Arrays

An array in scalar context evaluates to its size. You can easily get the index of the last item in an array.

```
my @s = ("milk","eggs","butter");
my $length = @s;
print "$length\n";
3

my @s = ("milk","eggs","butter");
my $last_index = $#s;
print "$last_index\n";
2

my @s = ("milk","eggs","butter");
print "$s[$#s]\n";
butter
```

Perl Arrays

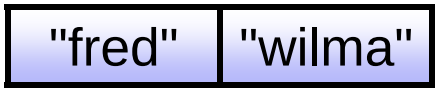
Special commands add or remove items to the front or back of arrays.
push and pop add to the back, making a stack.

```
my @s = ("milk","eggs","butter");
push @s, "beer";
print "@s\n";
milk eggs butter beer

my @s = ("milk","eggs","butter");
pop @s;
print "@s\n";
milk eggs

my @s = ("milk","eggs","butter");
my $last_item = pop @s;
print "$last_item\n";
butter
```

Perl arrays
grow or shrink as needed



@data

```
my @data = ("fred","wilma");
```

Perl arrays
grow or shrink as needed

@data

```
my @data = ("fred","wilma");
push @data, 42;
```

Perl arrays
grow or shrink as needed

@data

```
my @data = ("fred","wilma");
push @data, 42;
$data[5] = "dino";
```

undef

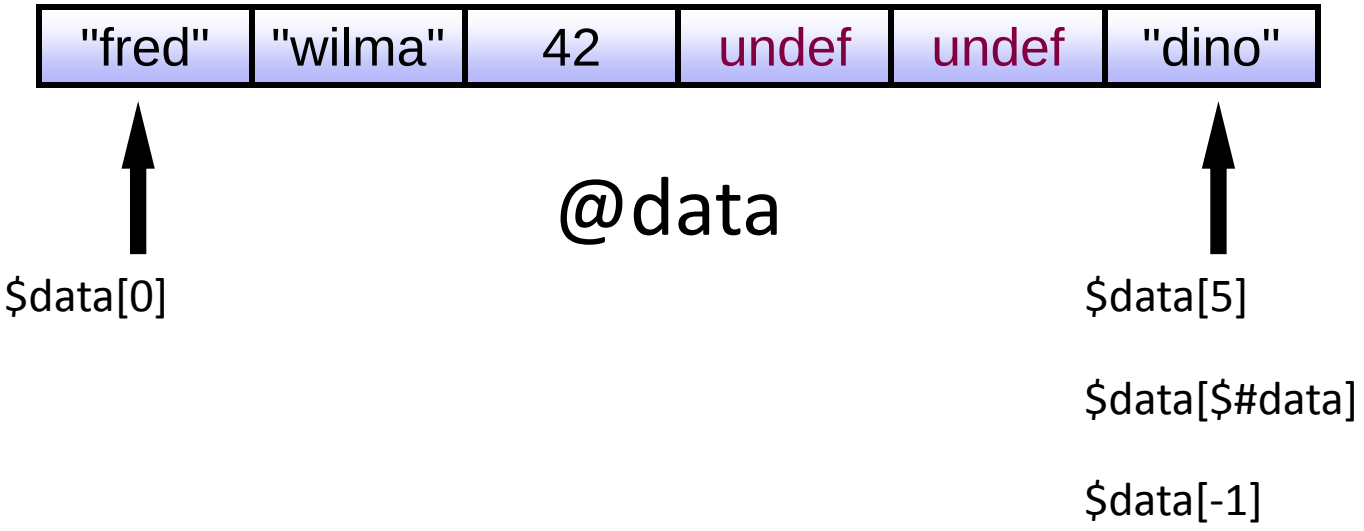
- The value of all uninitialized scalars (and scalar elements of arrays and hashes) has the special scalar value undef.
- undef evaluates as 0 when used as a number and "" when used as a string, which is why you most often don't have to initialize variables explicitly before you use them.

```
my $a; $a++; print "$a\n";
1
my @a = (1,2);
$a[3] = 23; print "@a\n";
Use of uninitialized value in join or string at test.pl line 4.
1 2  23
```

- Even after a scalar has been assigned, you can undefine them using the undef operator.

```
$a = undef;
undef @a;
```

Array indexing



Arrays and lists in assignments

@data

You can initialize or set arrays or lists by arrays or lists:

```
my ($man,$wmn) = ($data[0],$data[1]); print "$man $wmn\n";
fred wilma
my ($man,$wmn) = @data; print "$man $wmn\n";
fred wilma
@data = ("barney", "bambam"); print "@data\n";
barney bambam
my @mydata = @data; print "@data | @mydata\n";
barney bambam | barney bambam
```

You can swap elements without a temporary:

```
($data[1],$data[0]) = ($data[0],$data[1]); print "$data[0] $data[1]\n";
 bambam barney
```

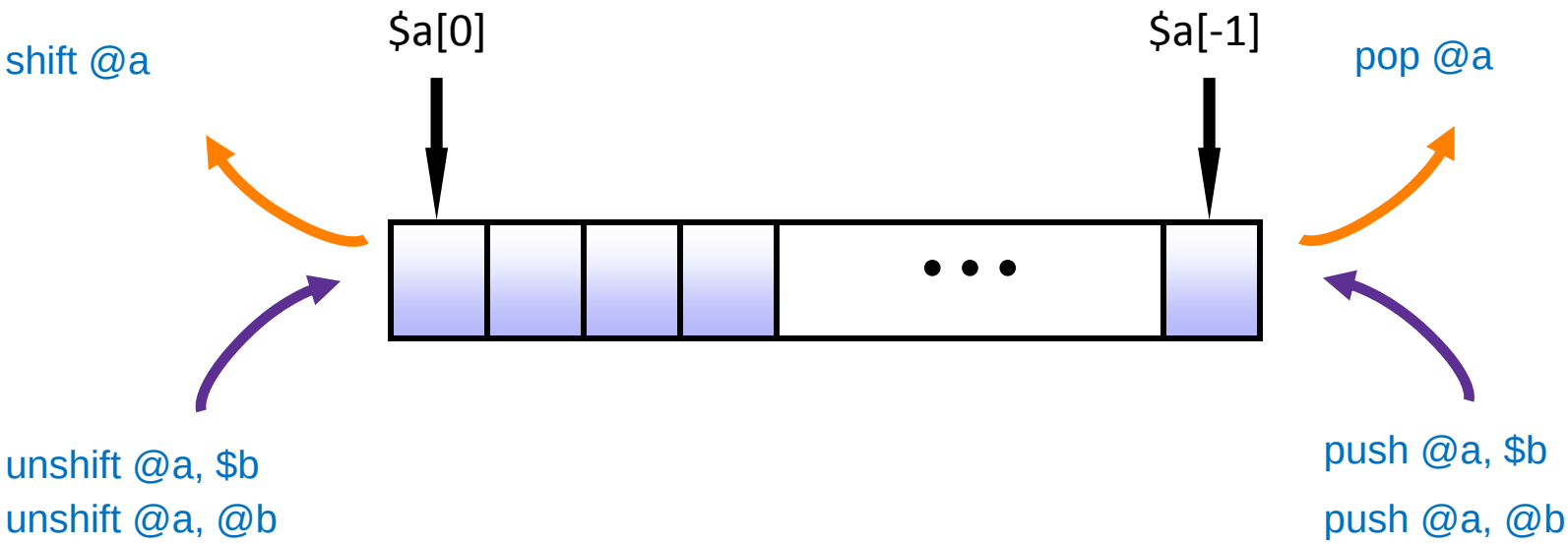
Array slices

@data

You can select multiple elements from an array at once.

```
my ($man,$wmn) = @data[0..1]; print "$man $wmn\n";
fred wilma
@data[2,3] = ("barney","bambam"); print "@data\n";
fred wilma 42 barney bambam dino
my @mydata = @data[0..2,5]; print "@mydata\n";
fred wilma barney dino
@data[0,1] = @data[1,0]; print "@data\n";
wilma fred 42 barney bambam dino
```

Adding elements to array ends



Loops: Iterating over Arrays

```
for ($i = 0; $i  < @data ; $i++) { # c-style
    print "$data[$i]\n";
}

for (0..$#data) { # perl-style, default scalar is index
    print "$data[$_]\n"; # use when you need the indices explicitly
    print "The $_","th element is $data[$_]\n"; # like here
}

foreach (@data) { # perl-stylier, default scalar is element...
    print "$_\n";
}

while (@data) { # evaluates false when scalar(@data) == 0
    print shift @data, "\n"; # side-effect: removes 0th element
}
```

conditions

- if – else statements are used to test whether an expression is true or false

```
if ($a < 0) {
        print "$a is a negative number\n";
} elsif ($a == 0) {
        print "$a is zero\n";
} else {
        print "$a is a positive number\n";
}
```

- Use the function defined to test if a scalar has the value undef

```
if (defined $a) {
        $a++;
}
```

equivalent to

```
$a++ if defined $a;
```

The rules of truth in Perl

- Only Scalars can be True or False
- undef is False
- "" is False
- 0 is False
- 0.0 is False
- "0" is False
- Everything else is True (including "0.0" !)

Logical expression

- $a == $b # compare numbers, true if $a equal to $b
- $a != $b # compare numbers, true if $a is not equal to $b
- $a eq $b # compare strings, true if $a is equal to $b
- $a ne $b # compare strings, true if $a is not equal to $b
- !$a # boolean, true if $a is 0, false if $a is 1

Controlling loops: next and last

next skip to the next iteration

```
my @a = (1,2,5,6,7,0);

my @filtered;
foreach (@a) {
    next if $_ < 5;
    push @filtered, $_;
}
print "@filtered\n";
```

```
5 6 7
```

last ends the loop

```
my @a = (1,2,5,6,7,0);

my $found_zero = 0;
foreach (@a) {
    if ($_ == 0) {
        $found_zero = 1;
        last;
    }
}
print "$found_zero \n";
```

```
1
```

Sorting arrays

- Use the built in function sort

- The results may surprise you!

```
my @words = ("c","b","a","B");
@words = sort @words;
print "@words\n";
B a b c

my @numbers = (10,3,1,2,100);
@numbers = sort @numbers;
print "@numbers\n";
1 10 100 2 3
```

sort

- sort uses a default sorting operator cmp that sorts "ASCIIbetically", with capital letters ranking over lower-case letters, and then numbers.

  sort @words;

  is equivalent to:

  sort {$a cmp $b} @words;

- cmp is a function that returns three values:
  - -1 if $a le $b
  - 0 if $a eq $b
  - +1 if $a ge $b
- where le, eq, and ge are string comparison operators.
- $a and $b are special scalars that only have meaning inside the subroutine block argument of sort. They are aliases to the members of the list being sorted.

sort {$a <=> $b} @numbers

- <=> (the "spaceship operator") is the numerical equivalent to the cmp operator:
  - -1 if $a < $b
  - 0 if $a == $b
  - +1 if $a > $b

- You can provide your own named or anonymous comparison subroutine to sort:

```
my @numbers = (10,3,1,2,100);
@numbers = sort {$a <=> $b} @numbers;
print "@numbers\n";
1 2 3 10 100
@numbers = sort {$b <=> $a} @numbers;
print "@numbers\n";
100 10 3 2 1
```

Syntax summary: scalars

- Declare: my $age;
- Set: $age = 29; $age = “twenty-nine”;
- Access: print “$age\n”; twenty-nine

Syntax summary: arrays

- Declare: my @children;
- Set all: @children = (“Troy”,”Anea”);
- Set element: $children[0] = “Troy Alexander”;
- Access all: print “@children\n”; Troy Alexander Anea
- Access element: print “$children[1]\n”; Anea

Syntax summary: loops

```
foreach my $child (@children) {
    print "$child\n";
}
```

```
Troy Alexander
Anea
```

```
for (my $i = 0; $i < @children; $i++) {
     print "$i: $children[$i]\n";
}
```

```
0: Troy Alexander
1: Anea
```

Syntax summary: conditions

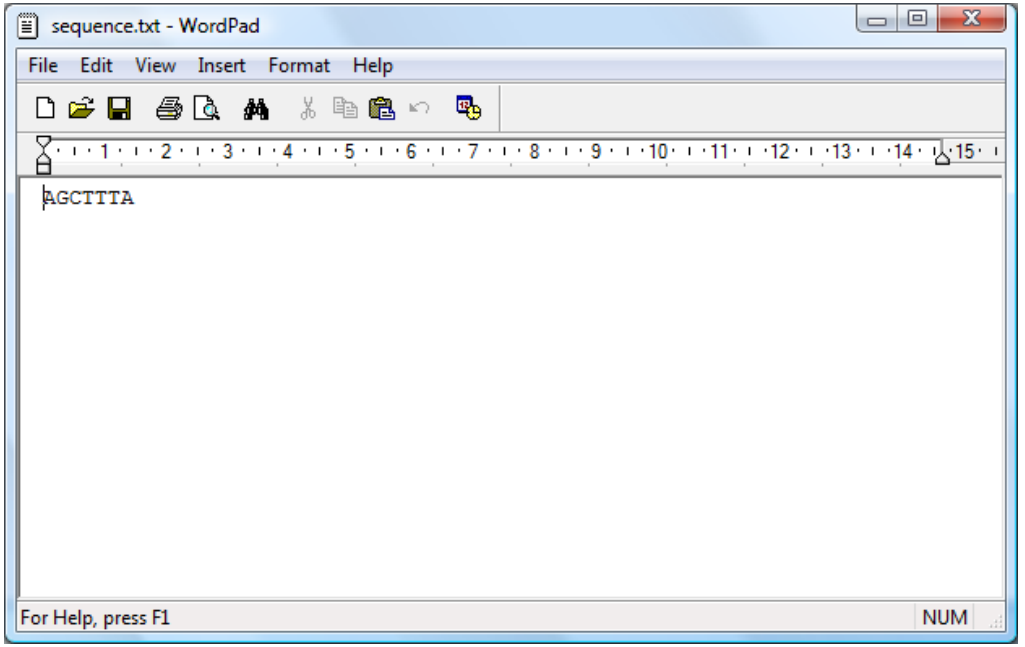
```
foreach my $child (@children) {
    if (length($child) > 4) {
        print "$child\n";
    }
}
```

Troy Alexander

Reading and writing to files

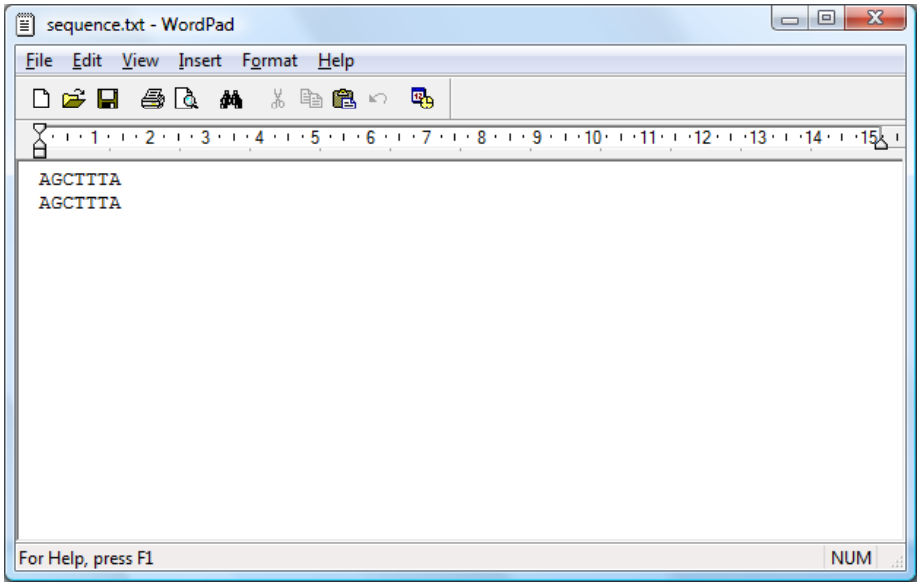
- open(A, ">sequence.txt") – creates a new file and opens it for writing
- open(A, ">>sequence.txt") – opens an existing file for writing
- open(A, "sequence.txt") – opens an allready existing file for reading

```
open(A , ">sequence.txt");
print A “AGCTTTA\n";
close(A);
```



Reading and writing to files

```
open(A , ">>sequence.txt");
print A "AGCTTTA\n";
close(A);
```




```
open(A , "sequence.txt");
my $line1 = readline *A;
my $line2 = readline *A;
close(A);
print "$line1 | $line2\n";
AGCTTTA
 | AGCTTTA
```

Reading files

```
my @seqs;
open(A , "sequence.txt");
while (<A>) {
    chomp;
    push @seqs, $_;
}
close(A);
print ”@seqs\n";
AGCTTTA AGCTTTA
```

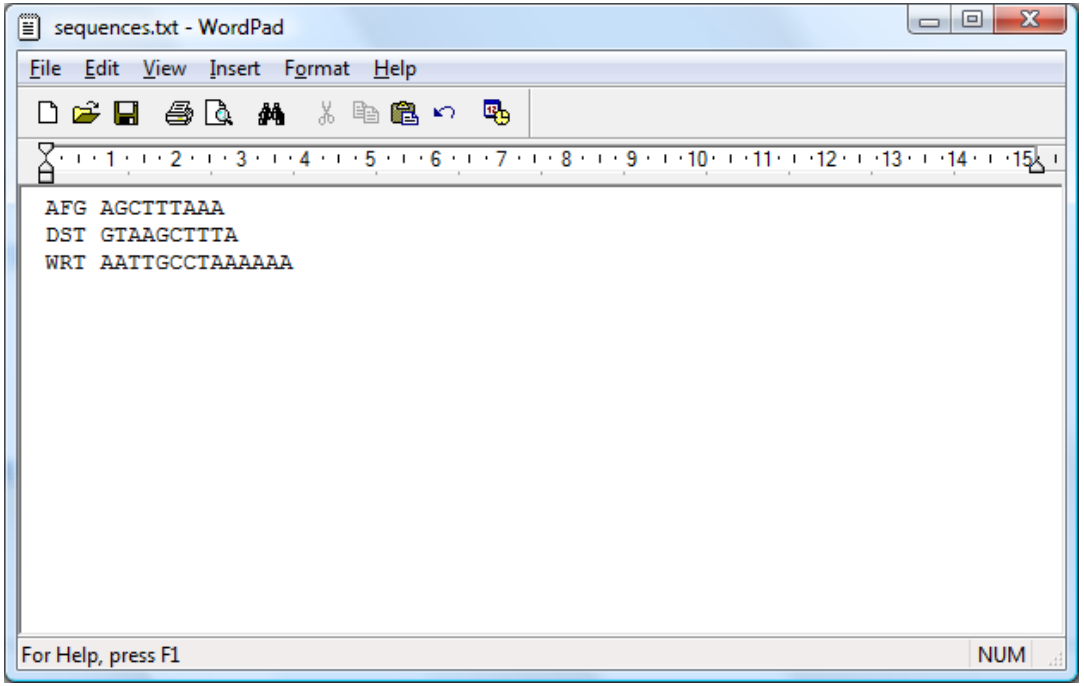
chomp removes ”\n” from the end of the line if it exists

Splitting strings: split

- You can split a string on any substrings that match a regular-expression with:
  - @array = split /PATTERN/, $string;
  - split /\s/, "do the twist"; # gives ("do","the","twist")
  - split //, "dice me"; # gives ("d","i","c","e"," ","m","e");

- Extremly useful when parsing files:

```
my @genes;
open(A , "sequences.txt");
while (<A>) {
    chomp;
    my ($gene) = split /\s/;
    push @genes, $gene;
}
close(A);
print ”@genes\n";
AFG DST WRT
```



Extracting fragments: substr

```
my $string = "AC Milan";
my $fragment = substr $string, 3;
print "$fragment\n";
```

```
Milan
```

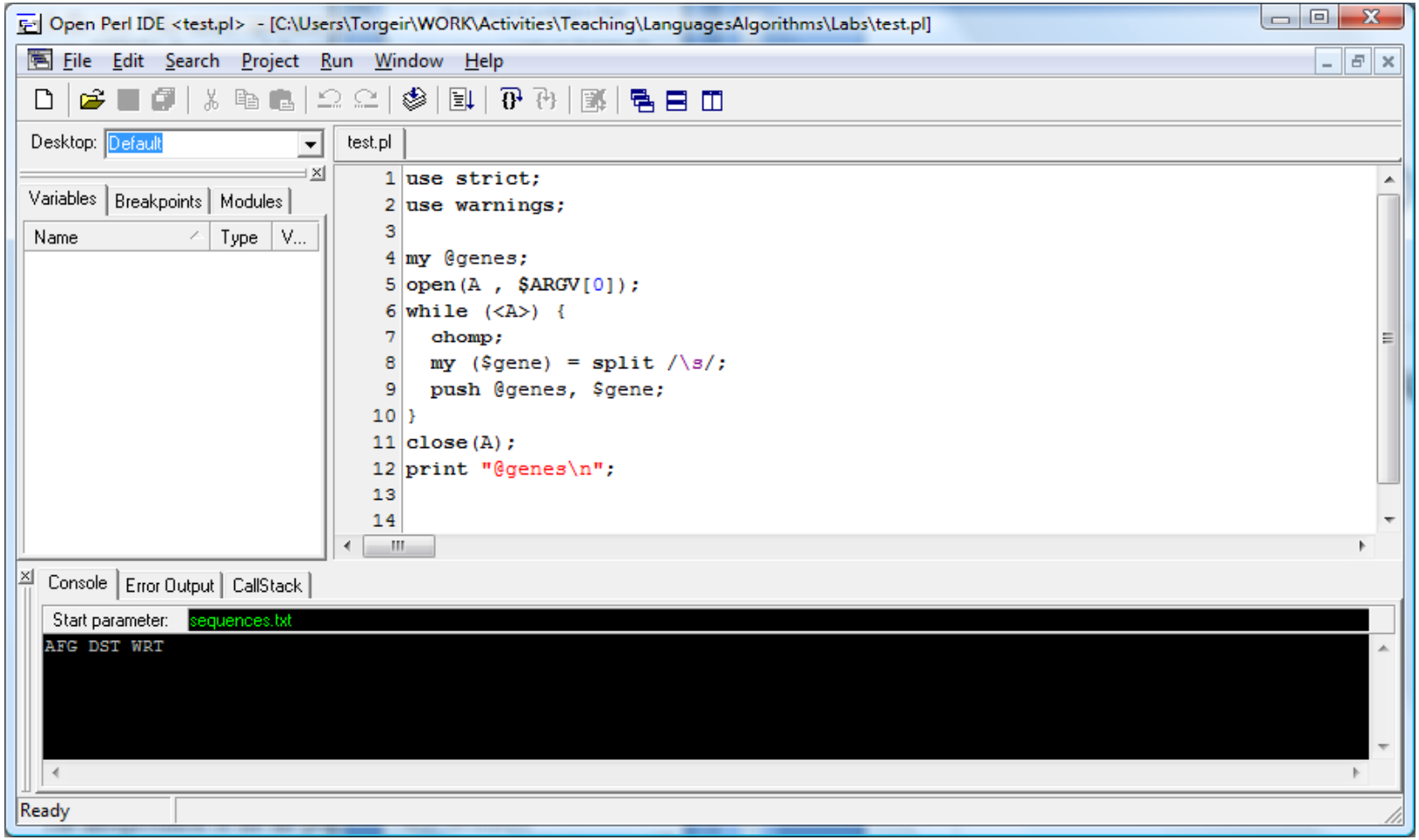
```
my $string = "F.C. Internazionale";
my $fragment = substr $string, 5, 5;
print "$fragment\n";
```

```
Inter
```

```
my $string = "F.C. Internazionale";
my $fragment = substr $string, -7, 4;
print "$fragment\n";
```

```
zion
```

@ARGV: command-line arguments



Acknowledgements

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