4.0.2.1.1

Sets and Spans

- handle coordinate elements
  - clones
  - contigs
  - alignments
- easily form intersections and unions of elements
- learn about index sets

Sets, Lists and Spans

A **set** is a finite or infinite collection of objects in which order is of no significance and multiplicity is usually ignored.

{1,2,5,10}

Common operations are membership ($\in$), intersection ($\cap$), union ($\cup$), or complement ($\overline{S}$). The empty set is $\varnothing$.

A **multiset** is a set in which multiplicity is explicitly ignored.

{1,1,2,5,10}

A multiset has the additional operation of multiplicity. A **list** is an **ordered** set of elements in which an object may be another set or multiset.

A **span of a set**, S, is defined as

$$\max S - \min S$$

A **span of elements**, E, is a set of consecutive objects

$$E(a,b) = \{x \mid a \le x \le b\}$$

A **window** on the integer line, for example.

Union of multiple sets is written as

$$\bigcup_{i=1,2,3} S_i$$

An intersection of multiple sets is written as

$$\bigcap_{i,1,2,3} S_i$$

An **index set** is a set whose elements label those of another set. Here K is the index set of S.

$$S = \bigcup_{k \in K} S_k$$

CPAN's offerings

- a large number of modules implement various aspects of sets, lists, etc.
  - do not write your own implementation – use these excellent resources

> we will focus on these

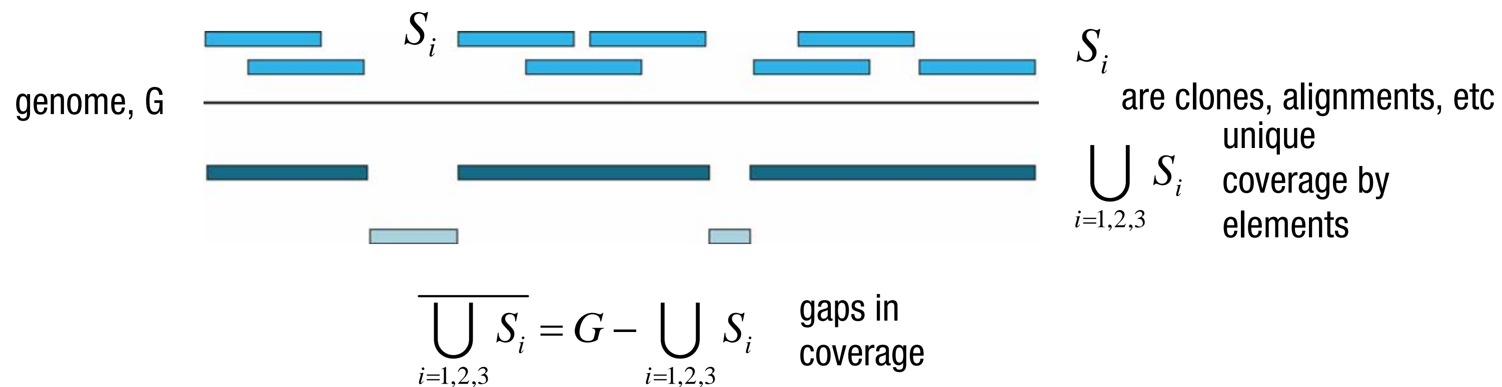
> and briefly look at these

	Module	DSLI	Description
	Set::Array	Rpd0p	Arrays as objects, with set methods
>	Set::Bag	Rpd0	Bag (multiset) class
	Set::CheckList	apdh	Maintain a list of "to-do" items
	Set::Crontab	Rpd0a	Expand crontab(5)-style integer lists
	Set::CrossProduct	Rpd0p	interact with the cartesian product of sets
	Set::Hash	Rpd0p	Hashes as objects, including set methods
	Set::Infinite	bpd0p	Infinite Set Theory module, with Date, Time
>	Set::IntRange	Rcd0p	Set of integers (arbitrary intervals, fast)
>	Set::IntSpan	Rpd0p	Set of integers newsrc style '1,5-9,11' etc
	Set::NestedGroups	Rpd0	Grouped data eg ACL's, city/state/country
	Set::Object	bcd0	Set of Objects (smalltalkish: IdentitySet)
	Set::Scalar	Mpd0p	Set of scalars (inc references)
	Set::String	Rpd0p	Strings as sets of characters
>	Set::Window	Rpd0p	Manages an interval on the integer line

search.cpan.org/modlist/Data_and_Data_Types/Set

Why You Should Care – Part I

- you work with objects that have **spatial coordinates** (alignments, clones, contigs, etc)
  - manipulate objects – intersection, union, difference
  - compute coverage, redundancy, gaps



$$\overline{\bigcup_{i=1,2,3} S_i} = G - \bigcup_{i=1,2,3} S_i$$ gaps in coverage

Why You Should Care – Part II

- you work with **indexed objects** (array probes), which may have spatial coordinates, and are interested in consecutive runs that exhibit a certain characteristic (experimental result)
  - 5 consecutive deleted array probes = putative deletion

probe index set 1 2 3 4 . . .
probe coordinate set P_1 P_2 P_3 P_4 . . .

run of 5 in index set of deleted probes

run of 6 in index set of amplified probes

- identify runs in index sets
- identify probes in runs
- extract coordinates of probes
- map runs to positions

```
D      := index set of deleted probes
R(D)   := all runs in index set
R(D,N) := all runs in index set of length N or greater
for r in R(D,N)
  # coordinate of first probe in run
  p = P(r->min)
  # coordinate of last probe in run
  q = P(r->max)
  # left position of probe run
  p->min
  # right position of probe run
  q->max
```

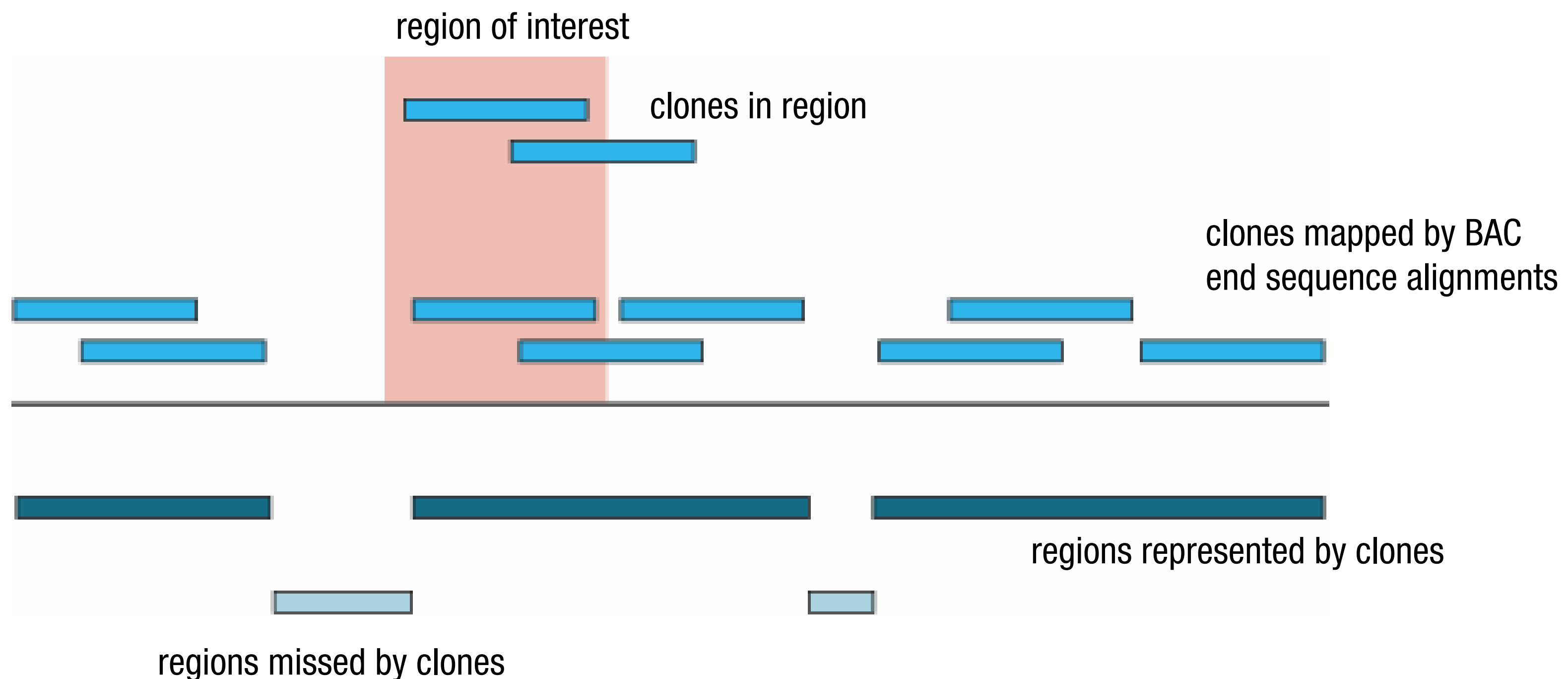
Set::IntSpan

- v1.08, Steven McDougall
- manages sets of integers, optimized for sets that have long runs of consecutive integers
  - supports infinite forms
    - (-5
    - 10-)
    - (-)
- spans operator is extremely useful in extracting runs from unions or intersections
- supports for iterators (first, last, next), comparisons (equal, equivalent, superset, subset)
- *very clean* API

```
$S = Set::IntSpan->new("1,5,10-15,20-50");
$T = Set::IntSpan->new("2-6,8-16,30-40,45");

$S->cardinality # 39
for $span ($S->spans) {
  $span->run_list     # 1  5  10-15  20-50
  $span->min          # 1  5  10     20
  $span->max          # 1  5  15     50
  $span->cardinality  # 1  1  6      31
}

$U = $S->union($T)
$U->run_list    # 1-6,8-16,20-50
$U->cardinality # 46

$V = $S->intersect($T)
$V->run_list    # 5,10-15,30-40,45
$V->cardinality # 19

$W = $S->diff($T)
$W->run_list    # 1,20-29,41-44,46-50
$W->cardinality # 20

$X = $S->union($T)->complement
$X->run_list    # (-0,7,17-19,51-)
$X->cardinality # -1
```

Set::IntSpan in Action

- I have some clones with end sequence coordinates and want to know
  - what parts of the genome to these clones represent?
  - given a genomic region, which clones lie entirely within this region? partially within the region?
  - are what are the largest “holes” in which no clones with coordinates can be found?

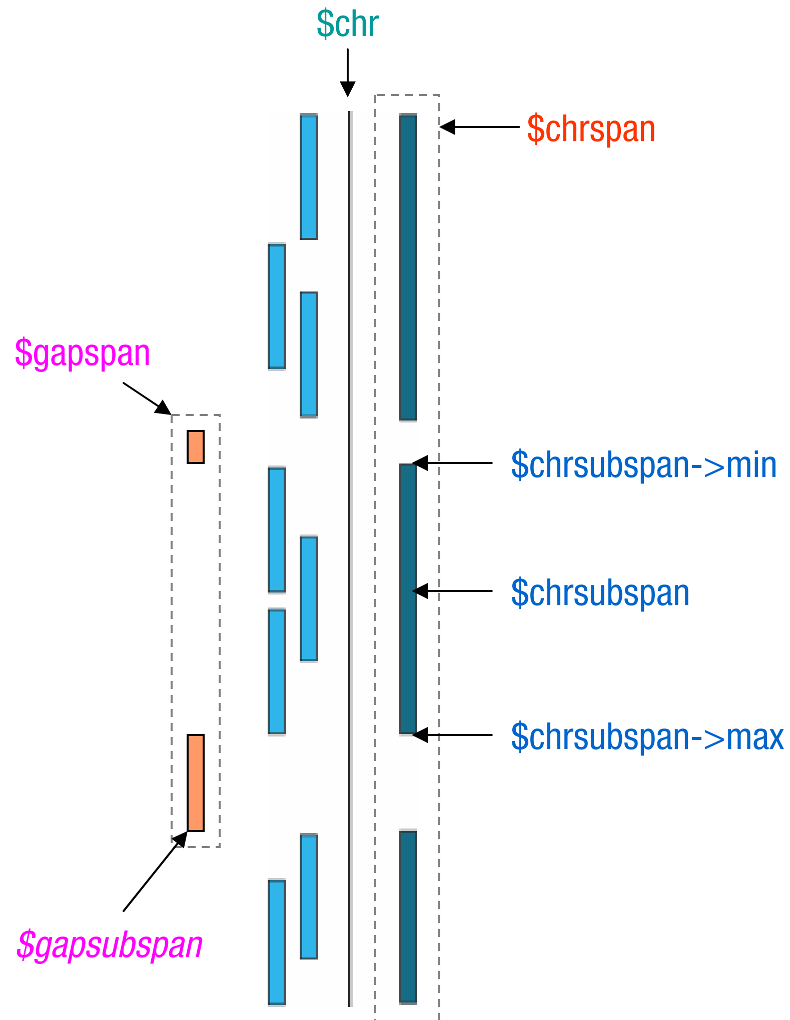


Constructing Spans from File Coordinates

- read coordinates from a file
  - construct a span for each clone
  - save the clone spans in an hash of arrays
  - construct a union of spans for each chromosome – on the fly
- $clonespans{$chr} reference to list of hashes
  - each hash stores clone name and clone span
- $chrspans{$chr} stores the union of all clone spans for a given chromosome

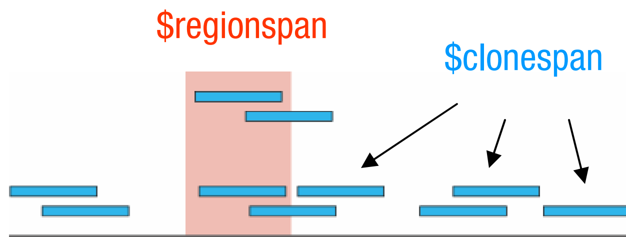
```
# clones.txt
#
# name chr start end
# RP11-2K22 1 238603586 238769410
# RP11-2K23 1 200117141 200294916
# RP11-2K24 1 63415083 63586024
#

open(F,"clones.txt");
my %chrspans;
my %clonespans;

while(<F>) {
  chomp;
  my ($clone,$chr,$start,$end) = split;

  my $clonespan = Set::IntSpan->new("$start-$end");

  $chrspans{$chr} ||= Set::IntSpan->new();

  $chrspans{$chr} = $chrspans{$chr}->union($clonespan);

  push(@{$clonespans{$chr}},
            {clone=>$clone,span=>$clonespan});
}
```

Determining Coverage by Coordinates




```
for my $chr (keys %chrspans) {
  my $chrspan = $chrspans{$chr};

  # total coverage on this chromosome
  $chrspan->cardinality;

  for my $chrsubspan ($chrspan->spans) {
    # contiguous regions of coverage
    $chrsubspan->cardinality;
    $chrsubspan->run_list;
    $chrsubspan->min;
    $chrsubspan->max;
  }

  my $entirechr = Set::IntSpan->new("1-$chrlength");
  my $gapspan = $entirechr->diff($chrspan);

  for my $gapsubspan ($gapspan->spans) {
    # regions missed by clone coverage
    $gapsubspan->cardinality;
    . . .
  }

}
```

Finding Overlapping Elements

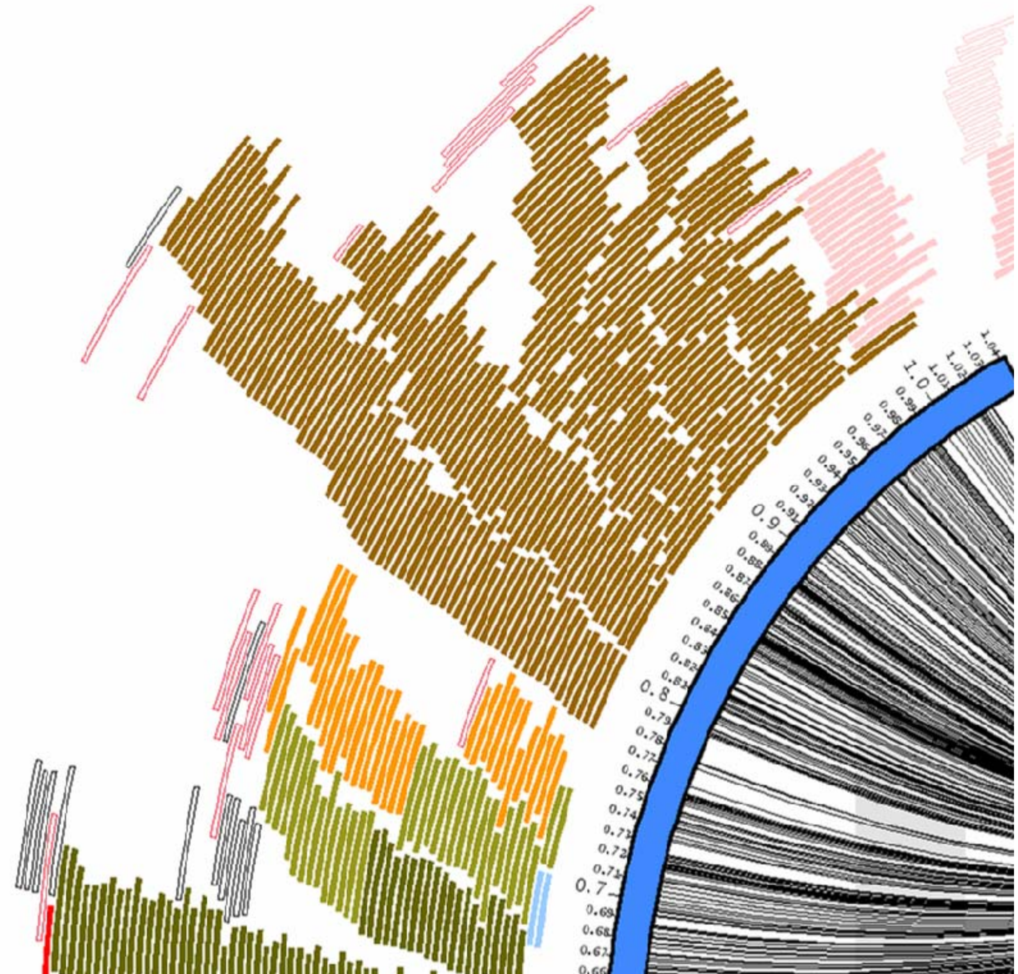


- do not test for non-empty intersection by using
  - if $a->intersect($b)
  - a span is always returned by intersect!
  - remember, you get a span object (therefore evaluates to TRUE) not the size of the span (which may be 0)
  - use
    - if $a->intersect($b)->cardinality
    - if not $a->intersect($b)->empty

```
my $regionspan = Set::IntSpan->new("$mystart-$myend");
my $regionchr = $mychr;

# do we have coverage on this chromosome?
if(exists $chrspans{$regionchr}) {

  # cycle through the clones on this chromosome
  for $clonespandata (@{$clonespans{$regionchr}}) {

    my ($clone,$clonespan)
         = @{$clonespandata}{qw(clone clonespan)};

    # intersect clone with region
    my $intersection =
       $clonespan->intersect($regionspan);

    # is the intersection non-empty?
    next unless $intersection->cardinality;

    # what fraction of the clone intersects the region?
    my $fraction = $intersection->cardinality /
                   $clonespan->cardinality;

    if ($fraction == 1) {
       # clone falls within region span
    } elsif ($fraction >= 0.5) {
       # most of clone falls within region span
    } else {
       # less than half of clone overlaps with region
    }

  }
}
```

Drawing Tilings

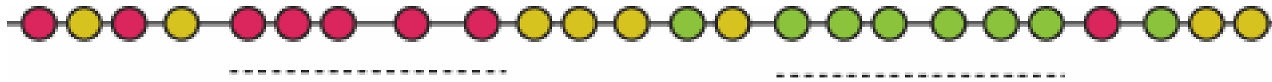
- did you ever wonder how tilings are drawn in genome browsers?
  - elements are drawn in layers, as not to overlap with one another in a given layer
- use Set::IntSpan
- set up N spans, one for each layer
- for each element to draw, find the first span, n, that does not overlap with the element
  - draw the element in layer n
  - add the element to the span,
    - span(n)->union(element)
  - you may want to pad the element to get small spacing



Index Sets

- sometimes intersect won't help you because your individual objects don't intersect (e.g. SNPs – single base pair positions)

- you are interested in consecutive runs of objects with a given characteristic



- suppose I have a collection of positions (e.g. SNPs from array)
  - each SNP has some identifier (name) and a value associated with it (-1, 0 or 1), for example.
  - let each SNP be represented by a HASH, keyed by **id**, **pos** and **value**.
  - assume all SNPs are on the same chromosome
    - if not, use a hash to store SNPs for each chromosome

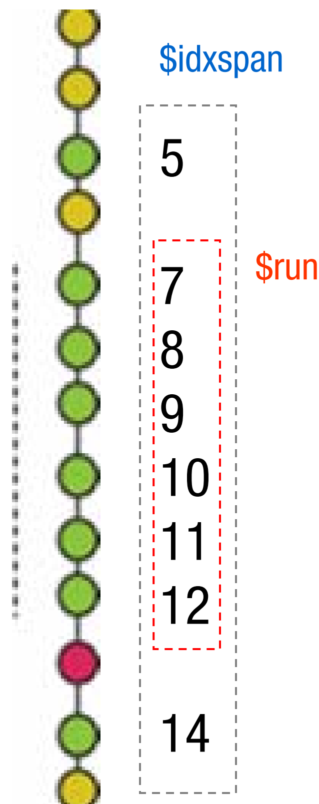
```
$snp = {id=>ID, pos=>POS, value=>VALUE}

$snp->{id}    # SNP_123
$snp->{pos}   # 23523829
$snp->{value} # 1
```

Associate Index with Each SNP

- we can’t intersect two SNP positions, since they’re single base pair coordinates
  - base pairs don’t overlap!
- neighbouring SNPs will have adjacent indeces
  - (i, i+1)
- runs of neighbouring SNPs with a given value will form a span
  - -1 SNPs
    - {1,5,6,7,8,9,20,25,28}
    - 1,5-9,20,25,28
- runs are identified by using the spans functions and testing the size of the span

```
# associate an index with each SNP,
# in order of appearance
my $idx=0;
for my $snp ( sort {$a->{pos} ⇔ $b->{pos}} @snp ) {
  $snp->{idx} = $idx++;
}

# let's make a idx-to-snp lookup table

my %idxtosnp;
map { $idxtosnp{$_->{idx}} = $_ } @snp;

# create three spans which will store index sets,
# one for each value of SNP

my @values = (-1,0,1);
my %idxspan;

map { $idxspan{$_} = Set::IntSpan->new() };

# populate each span with indexes of SNPs
# of a given value

for my $snp (@snp) {
  $idxspan{$snp->{value}}->insert($snp->{idx});
}
```

Identifying Runs of SNPs




```
# find runs of snps

for my $value (keys %idxspan) {

  # index set for a given SNP value (-1, 0, 1)
  my $idxspan = $idxspan{$value};

  # spans within index set (runs)
  for my $run ($idxspan->spans) {

    # test run size, make sure it's big enough
    my $runsize = $run->cardinality;
    next unless $runsize > 5;

    # what are the indexes in this run?
    my @runindexes = $run->elements;

    # recover SNPs in run
    my @runsnps = map { $idxtosnp{$_} } @runindexes;

    # SNP ids in run
    my @snpids = map { $_->{id} } @runsnps;

    # left and right most SNP positions
    my $leftpos = min ( map { $_->{pos} } @runsnps );
    my $rightpos = max ( map { $_->{pos} } @runsnps );

  }

}
```

Set::IntRange

- v5.1, Steffen Beyer

- this module is similar to Set::IntSpan, with additional features
  - you specify the maximum extent of your range
  - you "fill" elements with Bit_On/Bit_Off or Interval_Fill
  - overloaded operators
    - $U = $S * $T # intersection
    - $S *= $T # in-place intersection
    - $U = $S + $T # union
  - constructor takes a list, not a string
  - Norm instead of cardinality

Multiset – Grab Your Set::Bag

- v1.009, Jarkko Hietaniemi
- implements **multiset** – a set in which objects may appear more than once
- supports overloading
- use this when you want to keep track of multiplicity of elements of a given kind

```
$bag_1 = Set::Bag->new(sheep=>5,pigs=>3);
$bag_2 = Set::Bag->new(chickens=>2);

# add a sheep to bag 1
$bag_1->insert(sheep=>1);

# what animals are in bag 1?
@animals = $bag_1->elements;

# how many sheep?
$numsheep = $bag_1->grab("sheep");

# what's in the bag?
$bag_1->grab  # (sheep=>5, pigs=>3);

# eat a pig
$bag_1->delete(pig=>1);

# combine bags
$bag_1->insert($bag_2);
```

Window – Set::Window

- useful for implementing sliding windows
  - calculate GC content in 20kb sliding (by 5kb) windows

- Set::Window works similarly to Set::IntSpan, but represents a single run of consecutive integers
  - create a window using left/right position
  - move the window ($w->offset)
  - shrink the window ($w->inset(1000))
  - intersect windows ($w->intersect(@w))
    - largest window contained in $w and @w
  - union window ($w->cover(@w))
    - smallest window containing $w and @w
  - find windows inside a window ($w->series(5000))
    - get all unique windows of length 5000 within $w

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search. cpan. org

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Sets and Spans

- Set::IntSpan – get to know it
- explore CPAN's **Data and Data Types** section