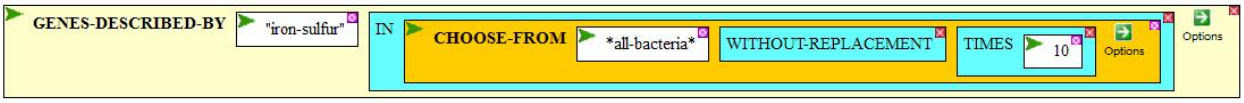
Pattern Matching

If you want to look for exact matches of a specific sequence (like all instances of "GAATTC" in a sequence) or almost exact matches (allowing some number of mismatches), then MATCHES-OF-ITEM or SEQUENCE-SIMILAR-TO (with MISMATCHES) will do the job. But sometimes your requirements are more complicated. Leaving bioinformatics for a moment, suppose you want to find all instances of telephone numbers in a page of text. You don't want addresses or stray numbers. By eye it's easy – just scan for something of the form of ###-####, where # is a digit. You're looking not for a specific sequence of characters but rather a ***pattern***. While humans are exquisite pattern finders, computers can be taught to look for well specified patterns also.

SQ1. Try this. Go to the VCU main web page (www.vcu.edu). Select and copy the entire page. Then go to any BioBIKE instance and bring down MATCHES-OF-PATTERN:

Mouse over the green action icon for the *target* entry box, click Multiline Input, and paste the page you copied between a pair of quotation marks. Click the Enter button to close the entry box. Then, open the *pattern* entry box and enter a pattern for telephone numbers: "###-####". Execute the function. Did you find telephone numbers? Go back to the web page and find them on the page. If you're not satisfied with the results, how can you change the pattern so that it excludes false hits?

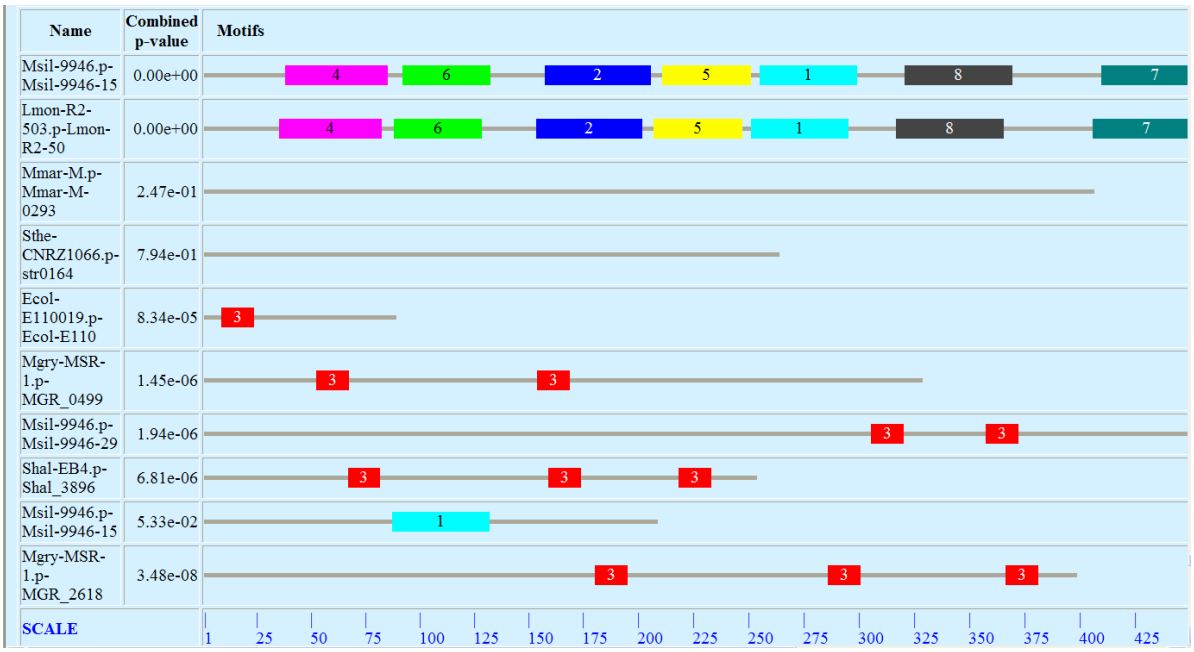
Similarly, it is often useful to find a pattern within a nucleotide or protein sequence. For example, suppose you're interested in certain proteins that catalyze oxidation-reduction reactions with the aid of an iron-sulfur coenzyme and want to be able to recognize their sequences. You could gather together a set of candidate proteins by looking for genes described by "iron-sulfur", but if you do, there's a good chance that in searching through the descriptions of every gene in every organism, you'll time out. Since you don't need an exhaustive list of such proteins but rather just a sampling, you can save time by getting the proteins from only a random subset of bacteria:



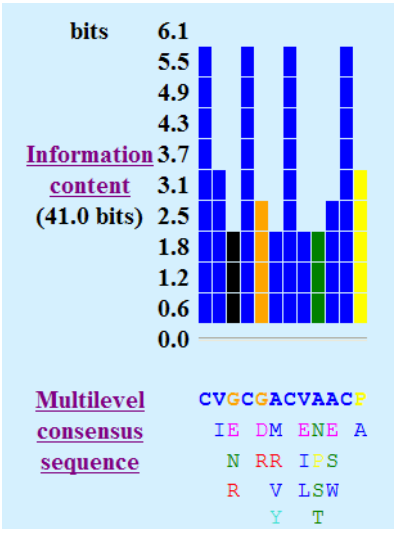
SQ2. Execute this function (in PhAnToMe/BioBIKE or replace *all-bacteria* with *all-cyanobacteria* and do it in CyanoBIKE). You'd like to get maybe 10-20 proteins. Do you get them through this function?

SQ3. Too many! Use the same CHOOSE-FROM trick to take a dozen of the proteins at random and find motifs within their sequences. Ask for 10 motifs. Anything interesting about the motifs?

Of course since you ran MOTIFS-IN with a quasi random set of iron-sulfur proteins, you'll get somewhat different results than I did, but you'll probably see something like this:



Scrolling up to the third motif, I find the remarkable consensus sequence and information profile shown at the right. In this motif, none of the amino acids are conserved except for four cysteines, and they're conserved 100%! It looks like these proteins annotated as iron-sulfur proteins have little similarity to one another except for a motif of **C**C**C***C**, where * denotes any amino acid.



Searching for this motif might lead me to other iron-sulfur proteins, but how to find them? Blast would be totally useless. It requires regions of contiguous similarity. Perhaps this is a job for MATCHES-OF-PATTERN? You think?

SQ4. Use MATCHES-OF-PATTERN to look for iron-sulfur oxidation-reduction proteins IN-EACH of the PROTEINS-OF a bacterium of your choosing (either in PhAnToMe/BioBIKE or CyanoBIKE). Use the pattern found above ("CC**C***C"), RETURN 1 match for each protein found, and make sure the matches are LABELED. From the result, extract the proteins using the FIRST IN-EACH function, and display the DESCRIPTIONS-OF EACH of the proteins. Was the strategy effective in finding the desired proteins?**

So far, the patterns you've seen have made use of sets of characters (# = digits) and wild-cards (*), but pattern matching goes well beyond that. Perhaps now is the time to visit the summary of

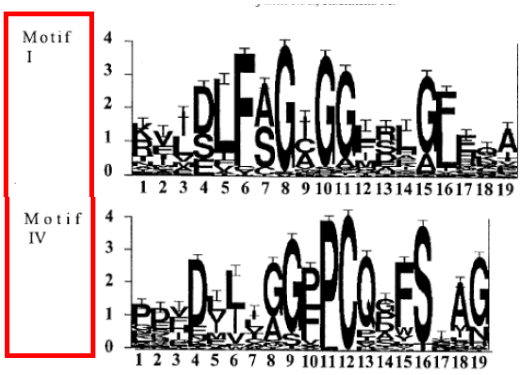
conventions used by pattern matching in BioBIKE (see link on the calendar). The first table shows the two character set characters you've already used (# and *****), but you see that several others are defined and that it is possible to devise any character set you like, using the **[ ]** tool. For example, it may be useful to make up a character set [ACGT], the set of all possible nucleotides or its negative [~ACGT].

SQ5. You've always had your doubts about the cyanobacterium *Synechococcus* BL107, which you've suspected of having a ratty genome. Test this out, using MATCHES-OF-PATTERN "[~ACGT]" to determine if there are any parts of the genome sequence composed of letters besides the four nucleotides. If you find such a region, follow it up by examining the sequence (using SEQUENCE-OF) to see if at least one of the position(s) identified by MATCHES-OF-PATTERN really does have a nonstandard letter.

The second table on the list shows ways of specifying repetition. For example:

SQ6. Look for candidate transcriptional terminators in phage TP901-1. You'll recall that a certain type of transcriptional terminator characteristically has a gapped palindrome followed by a run of at least 5 T's. The palindrome you'll need to recognize by eye (at least for now), but MATCHES-OF-PATTERN can certainly help. Search the set of downstream sequences of TP901-1 using a pattern consisting of 20 nucleotides followed by five or more T's ("*{20}T{5,}"). Try this out with the SEQUENCE-DOWNSTREAM-OF one gene (say the first gene of TP901-1), then generalize to all genes of the phage. Find any reasonable candidates for transcriptional terminators?

Most of your projects concern particular proteins with one goal as learning how to identify them in the proteins of incompletely annotated phage genomes. I provided a sample research project of this type. You'll recall that I found a description of motifs of cytosine-specific DNA methyltransferases, part of which is shown to the right. If I focus on just the most conserved amino acids, I can use these motifs as a basis for searching for proteins of this class in organisms I'm interested in.



SQ6. Devise a pattern that contains the four most conserved amino acids of Motif I as well as the two most conserved amino acids of Motif IV. Combine them into a single pattern separated by a indeterminate gap ("*…"). Use MATCHES-OF-PATTERN to find proteins with this pattern within the genome of A7120 (in CyanoBIKE or PhAnToMe/BioBIKE). RETURN only one match and ask that the result be LABELED with the name of the protein. Extract from the result the proteins matched, using the FIRST function as before. Then display the descriptions of the proteins (with LENGTH of 100 to allow the full description to be shown. From clues in the sequence and motifs, could you have picked out the proteins that are truly DNA methyltransferases and excluded the others?