

1.

- Today I will talk about my project.
- The topic of my project is about development of a new structure abstraction, we call it as "helices indices of RNAs"
- If you have some questions during my presentation, feel free to interrupt me.

2.

I've divided my presentation into 4 parts

- in the first part, I will talk about the basic secondary structure elements of RNA and introduce a classical RNA secondary structure prediction algorithm
- because the concept of "helices indices of RNAs" is based on the concept of "abstract shapes", that was developed by Bjoern, so I will introduce the concept of "abstract shapes" in the 2nd part.
- give the basic idea about the helices indices.
- in the last part, I will give an outlook of the project

3.

- In this slide, I will talk about the basic secondary structural elements of RNA,
- As the figure showed, RNA is composed of 2 kinds of elements, like 6 种.  
the first kind is energy favorable part, it includes dangling end and base stacking
- such energy favorable elements lead to formation of energy unfavorable elements, they are 4 种.
- all double stranded regions are also called as 'helices', it is always related with a loop type.  
for example we call this part as helices of hairpin loop, this part as helices of multiloop, this part as helices of bulge loop, this part as helices of internal loop.
- the concept is very important, because we will develop a new methods that based on the helices. I will explain it later in this presentation in more detail.

4.

- In this slide, I will introduce the classic algorithm for RNA secondary structure prediction. namely Zuker algorithm. The algorithm was first described by Zuker and Stiegler in 1981.
- the basic idea is sequence can be folded into many different secondary structures.  
furthermore, we can calculate for every secondary structure a unambiguous free energy value by adding the free energies of all elements of the secondary structure.  
after that, the algorithm choose the structure with the minimum free energy.
- The runtime of the algorithms is  $O(n^3)$  where  $n$  is the length of sequence,
- From this algorithm, we can get only one solution.

5.

- To better understand it, I prepared a small example,
- as I just said, in Zuker algorithm, for every secondary structure we calculate a free energy value by ...
- as the figure shows, the secondary structure consists of a hairpin loop, dangling end, 2 base stacking, a bulge loop,
- among them, the hairpin loop and dangling end are energy favorable, they have the negative free energy, and in contrast, hairpin loop and bulge loop are energy unfavorable, they have positive free energy.
- after addition of all elements, we get a free energy for the whole secondary structure, namely -4.6 kcal/mol.

6.

- if we calculate free energy for every secondary structure and draw it on a graph, we get a landscape.

- as the figure showed, the x-axis means conformations,  
the y-axis means free energy,  
if a RNA molecule don't have conformational switch, typically, if we see it from the landscape, the energy difference between minimum free energy and energy of the first sub-optimal confirmation is enough big.
- In Zuker algorithm, we calculate only this point.

7.

- aber in practice, the native structure is not always the one 照读...
- what can we do to find the native structure? One of solutions is that we define a range and enumerate all suboptimal 照读...

8.

- the figure shows the idea I just explained last slide, firstly, we define a linie in the energy landscape and calculate all suboptimal structure under the linie.
- but it caused another problem, namely the number of suboptimal structures grows exponentially with the size of the energy range.
- How can we solve the problem?

9.

- 照读: One of the solution is further classify ...  
abstract shape is one solution in the direction.  
it was developed by ... initial ideas ...
- central to this approach is ...  
for example in abstract shape type 5, all loops excepts for internal loop and multiloop are abstracted.
- each shape has a representative structure called shrep. It is the structrue with the minimum free energy within the shape class.

10.

- this figure shows an output example from abstract shapes by setting an envergy range of 5 kcal/mol above the mfe.
- the picture above is 2 dimension representation, the picture below is the textual output.
- from the intuitive perspective, every nested square brackets in abstract shapes corresponds to a branch in 2 dimensions representation, for example in the record 3, it has 3 branches in picture above, it has also 3 nested square brackets in abstract shapes, it is one-to-one correspondence
- in the middle of the record: shrep structure
- on right side: free energy of shrep

11.

- the abstract shape works pretty well, but one drawback is still there. namely 照读.
- What is consequence of the drawback?
- To explain the drawback, I prepared an example, as the figure shows, although the abstract shape above and below are identical, but position of the hairpin loop are totally different.
- the drawback make 照读...

12.

- for the reason we will develop a new structure abstraction namely helices indices. It includes the information of positions of helices.
- to develop it, 2 things have to be decided,
- the first thing is Which secondary structure element should be recorded?
- we have 4 candidate ...
- the second point is which position of this element should be recorded?
- we have also 4 candidates,  
i is first position of helix, j is last position of helix,  
we can also record the both positions at the same time or the central position of them.

13.

- To better understand it, I prepared a small example,
- In this example, We record only hairpin loop and use the central position
- So as the figure showed, the structure is composed of 2 helices, namely this one and this one.  
because we abstract from the bulge loop, so we don't consider this part.
- the position of i is 8, j is 13,  $i+j/2$  is 10.5, similarly, k is 35 and l is 41, and  $k+l/2$  is 38. Therefore, this structure would be abstracted to [10.5, 38].

14.

- the slide showed 照读
- in this example, we record multiloop and hairpin loop and use the central position, among them, the multiloop is marked with the letter 'm'. for example, in the record, 30m means the position comes from a multiloop.
- the most interesting information from the list hide in 3 records, namely this one, this one and this one
- if we compare the 3 records, we can find the helices indices of this record is a combination of the first 2 records.
- what does it mean? the answer is in the next slide.

15.

- if we draw the 3 records in energy landscape, it must be like this.
- the first record is global minimum structure and the second record is a local minimum. They have almost the same free energy.
- furthermore, the combination records is a saddle point
- so if we move from this point to this point, we have to pass the saddle point. Because the free energy of all 3 helices indices are known, therefore, we can calculate the difference easily. the difference is barrier energy.
- in our example, (返回去), the mfe-point has energy 10.7, this point has energy 2.3, and the barrier energy is about 8.4

16.

- from this slide, I will talk about the first problem we encountered, this is a runtime problem.
- the figure shows 照读  
in the figure, x axis is sequence length, y axis is number of helices indices or abstract shapes  
the line means the helices indices space, the line means the abstract shapes space.
- we notice, 照读, therefore it caused a runtime problem. In practice, for a sequence with 72 nucleotides, we need about 32 hours to calculate the helices indices on our super computer, it is not satisfactory.
- how can we solve this problem?

17.

- one solution is that 照读,
- the figure shows 照读
- there are altogether 5 lines in the figure  
the first line means the helices indices without energy limitation  
second is with a energy limit of 20 kcal/mol, this is with 15, this is with 10, this is with 5.
- although all helices indices space grow exponentially with sequence length, but the degree of steepness are different,
- the tendency is the lower the energy range, the flatter the line and the better the runtime will be.
- so if we set a very low energy range on the calculation, we will get a better runtime and solve the problem.

18.

- in last slide, I will give an outlook of the project.
- at first, we will develop a new structure abstraction, namely the helices indices
- after that, the idea will be implemented based on the idea.
- of course, the software will be evaluated by benchmark program
- lastly, we will design a RNA class predictor

19.

Thank you for your attention!  
Are there any questions?

questions:

1. How was implemented the idea in detail?

dynamic programming is a method for solving complex problems by breaking them down into simpler subproblems.

The key idea behind dynamic programming is quite simple. In general, to solve a given problem, we need to

solve different parts of the problem (subproblems), then combine the solutions of the subproblems to reach an overall solution.

Often, many of these subproblems are really the same. The dynamic programming approach seeks to solve each subproblem only once,

thus reducing the number of computations. This is especially useful when the number of repeating subproblems is exponentially large.

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2. Why is mfe structures not the native one?

This can be explained by the existence of modified bases in native tRNAs, which leads to the formation of a structure that is not the optimal under the energy model used.

3.

It exists a software, it can analyse the folding space completely. Only the runtime of the program is very bad.

This is also the reason why we will develop a new program because we will improve the runtime.

4.

- In this algorithm, we have to assume one condition, namely we get away the knots from the calculation.

The reason why we can get away the knots from the calculation is the calculation result of secondary structure prediction are used to infer

3-dimensional structures and knots can be inferred at this stage as well.