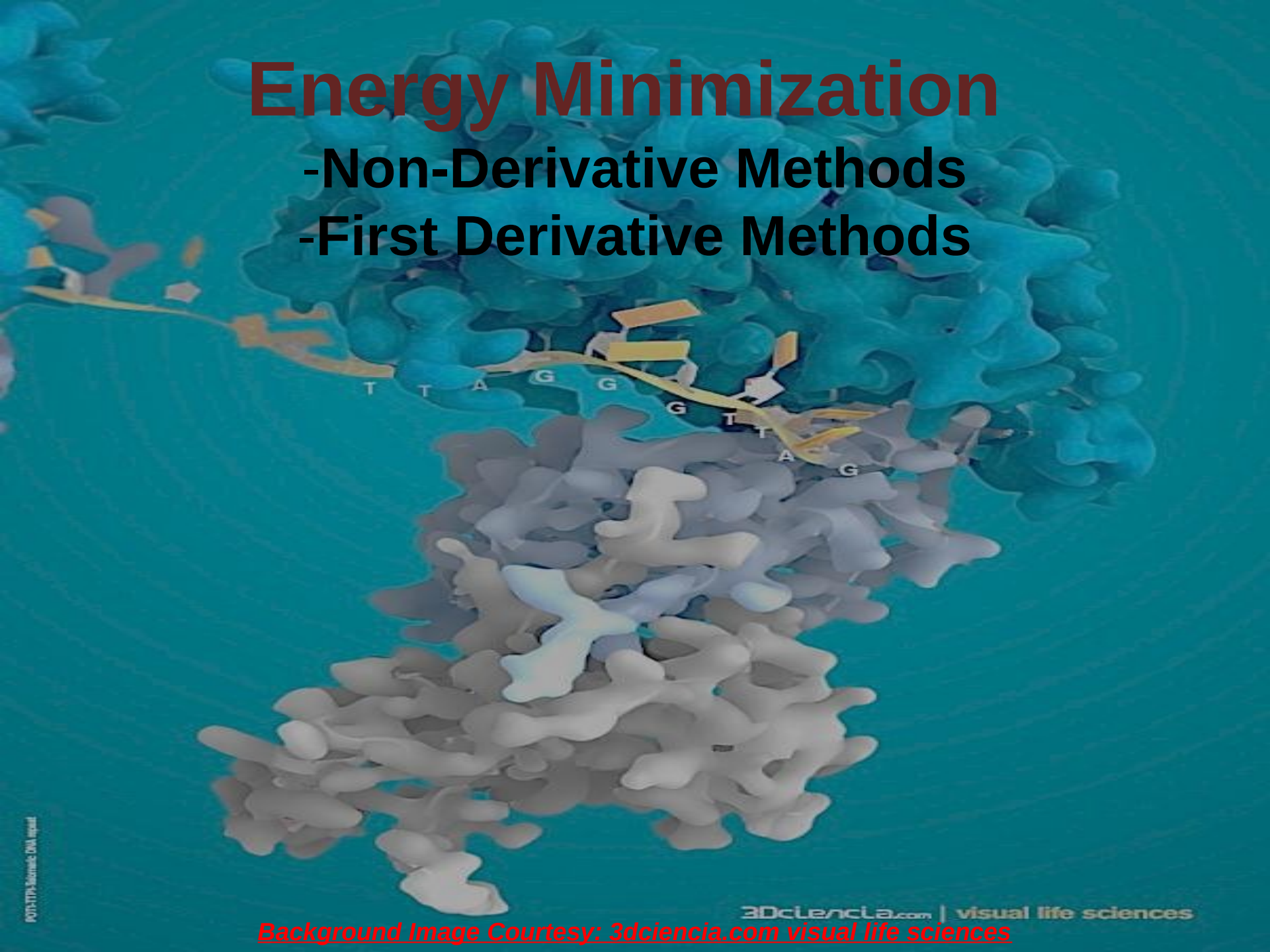
Energy Minimization

-Non-Derivative Methods

-First Derivative Methods



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Contents

- Introduction
- Criteria to start minimization
- Energy Minimization –The Problem
- Non Derivative Methods
  - Simplex Method
  - Sequential univariate method
- First Derivative Methods
  - Steepest Gradient
  - Conjugate Gradient Method
- References

Introduction

- The lowest energy conformation is the set of bond lengths and angles that gives the smallest steric energy.

- In other words, bonds find a compromise among competing forces to determine the lowest energy conformation.

- The goal of molecular mechanics is to determine the lowest energy conformation of a molecule. The process is called **energy minimization** [1]

- Knowing the stable conformers of a molecule is important because it allows us to understand its properties and behavior based on its structure [2]

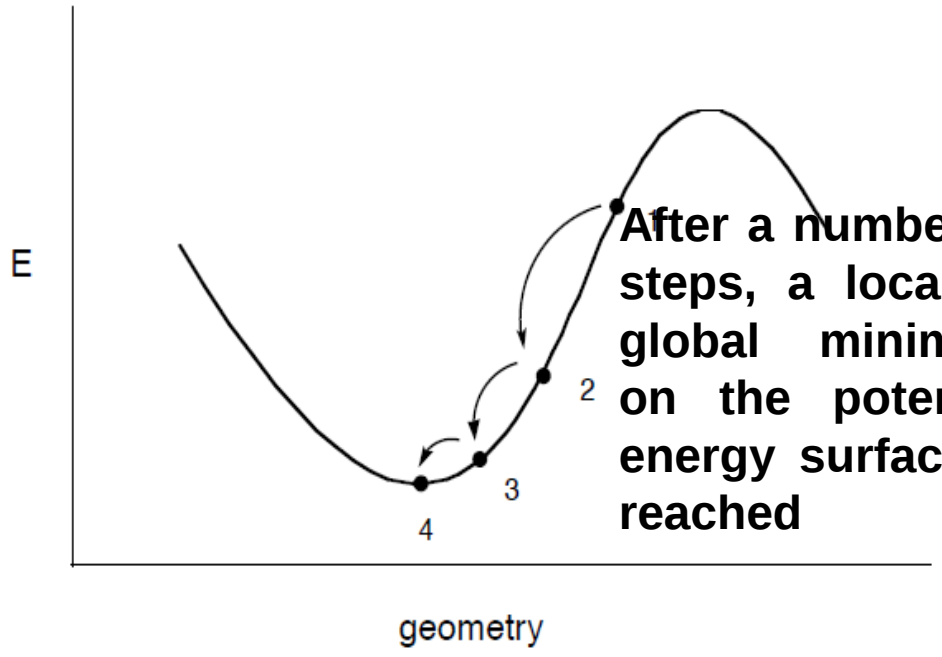


Figure 1. The process of energy minimization changes the geometry of the molecule in a step-wise fashion until a minimum is reached.

After a number of steps, a local or global minimum on the potential energy surface is reached

General Formula:

$$x_{new} = x_{old} + correction$$

xnew **- the value of the geometry at the next step**

Xold **- refers to the geometry at the current step**

correction **- some adjustment made to the geometry**

In all these methods, a numerical test is applied to the new geometry to decide if a minimum is reached. For example, the slope may be tested to see if it is zero within some numerical tolerance. If the criterion is not met, then the formula is applied again to make another change in the

Criteria to start minimization

1. Starting set of atomic coordinates
2. Parameters for various terms of the potential energy function [3]
3. Description of molecular topology

Energy Minimization –The Problem

- **E = f(x)**
- **E - function of coordinates Cartesian /inte**
- **At minimum the first derivatives are zero a**

  the second derivatives are all positive

$$\frac{dE}{dx_i} = 0$$

$$\frac{d^2E}{dx_i^2} > 0$$

- **Derivatives of the energy with respect to the coordinates provide information about the shape of energy surface and also enhances the efficiency of the minimization. [5]**

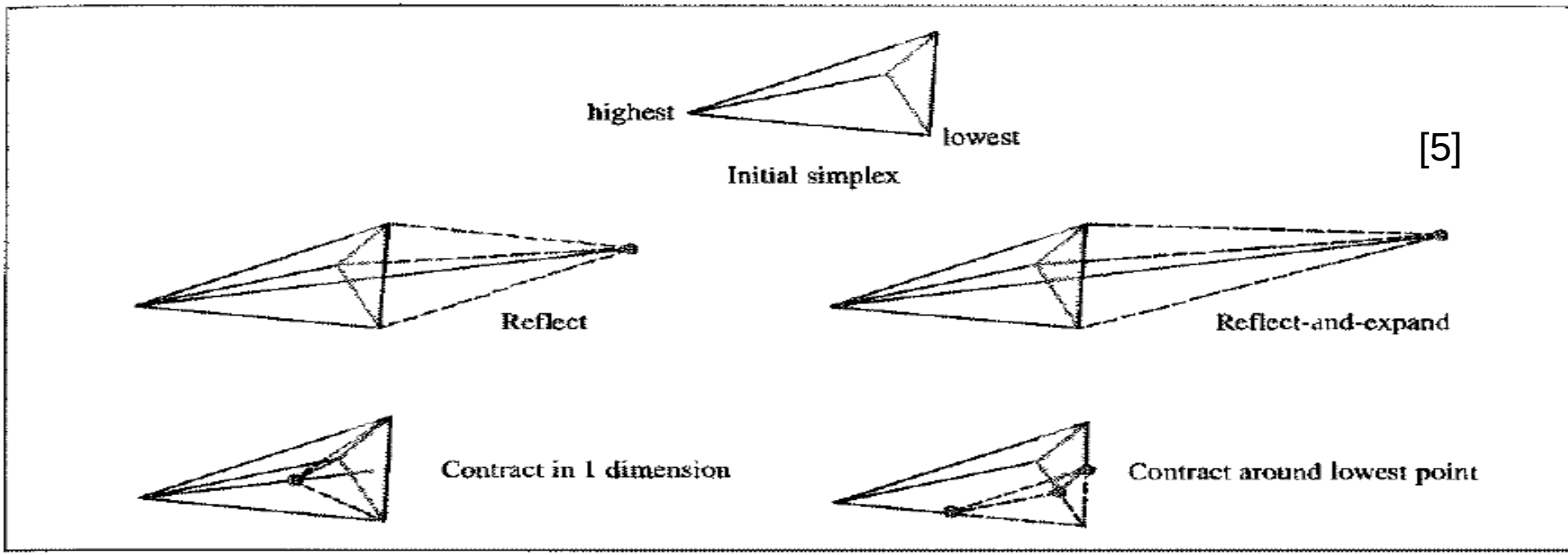
- **A Hessian matrix is a square matrix of second derivatives of a**

Non Derivative Methods

– Require energy evaluation only and may require many energy evaluations

–– Simplex Method

- Simplex is a geometrical figure with M+1 interconnected vertices, where M is the dimensionality of the energy function
- It does not rely on the calculation of the gradients at all.

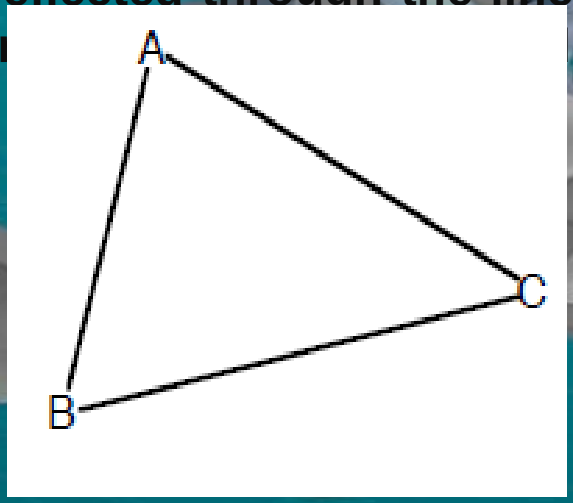


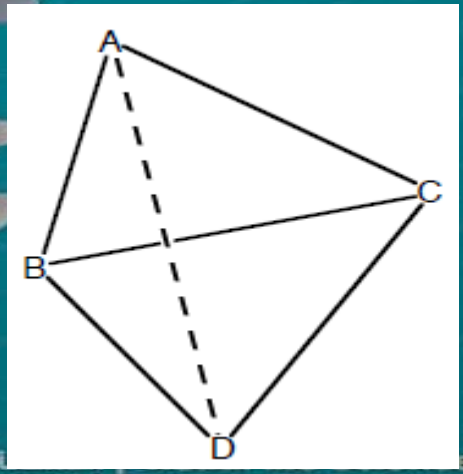
[5]

Fig 5.4: The three basic moves permitted to the simplex algorithm (reflection, and its close relation reflect-and-expand; contract in one dimension and contract around the lowest point) (Figure adapted from Press W H, B P Flannery, S A Teukolsky and W T Vetterling 1992. Numerical Recipes in Fortran. Cambridge, Cambridge University Press.)

- To implement the simplex algorithm it is first necessary to generate the vertices of the initial simplex.
- The initial configuration of the system corresponds to just one of these vertices. The remaining points can be obtained by adding a constant increment to each coordinate in turn. The energy of the system is calculated at the new point, giving the function value for the relevant vertex. [5]

- The point with the highest energy of the three is noted. Then, this point is reflected through the line segment connected the other two (to move away from the region of high energy).
- If the energy of point A is the highest out of the three points A, B and C, then A is reflected through line segment BC to produce point D.
- In the next step, the two original lowest energy points (B and C) along with the new point D are analyzed. The highest energy point of these is selected, and that point is reflected through the line segment connecting the other two. The process contin ocated. [2]





- **The sequential univariate method is a non-derivative method that is considered more appropriate as it systematically cycles through the coordinates in turn**
- **For each coordinate, two new structures are generated by changing the current coordinate.**
- **The energies of these two structure are calculated.**
- **A parabola is then fitted through the 3 points corresponding to the two distorted structures and the original structure.**
- **The minimum point in this quadratic function is determined and the coordinate is then changed to the position of the minimum**

[5]

Derivative Methods

- The direction of the first derivative of the energy (the gradient) indicates where the minimum lies, and the magnitude of the gradient indicates the steepness of the local slope.
- The energy of the system can be lowered by moving each atom in response to the force acting on it; the force is equal to minus the gradient.
- Second derivatives indicate the curvature of the function, information that can be used to predict where the function will change direction (pass through a minimum or some other stationary point) [5]

When discussing derivative methods it is useful to write the function as a Taylor series expansion about the point x_k:

$$\mathscr{V}(x) = \mathscr{V}(x_k) + (x - x_k)\mathscr{V}'(x_k) + (x - x_k)^2\mathscr{V}''(x_k)/2 + \cdots \qquad (5.2)$$

- When discussing derivative methods it is useful to write the function as a Taylor series expansion about the point Xk
- Therefore first order methods use the first derivatives (gradients),

Steepest Descent

Conjugate Gradient

Steepest Descent

- In the steepest descents method, the Hessian is just approximated as a constant, γ

- γ as an effective force constant and is calculated at the beginning of the first step to give a specified step size. [1]

$$x_{new} = x_{old} - \gamma E'(x_{old})$$

γ is a constant

- In this method, the gradients at each point still must be calculated, but by not requiring second derivatives to be calculated.

- The method is much faster per step than the Newton-Raphson method

Conjugate Gradient Method

- Conjugate gradient is a variation of the steepest descents method. The calculation of the gradient is improved by using information from previous steps. [1]
- The gradients of the current geometry are first computed. The direction of the largest gradient is determined after the gradient of current geometry is computed.
- The geometry is minimized along this one direction (this is called a line search). Then, a direction orthogonal to the first one is selected (a [illegible]n). The geometry is minimized along this direction.
- [illegible] the geometry is optimized in all the directions.
  - Pure steepest descents algorithms always take 90° turns after each stage, which may move the first minimization stage away from the optimal value.
  - If the initial steepest descents finds the minimum along the initial direction. The next best direction to look for the overall minimum is not necessarily perpendicular to the initial path.
  - Conjugate gradients is a good general purpose technique. [2]

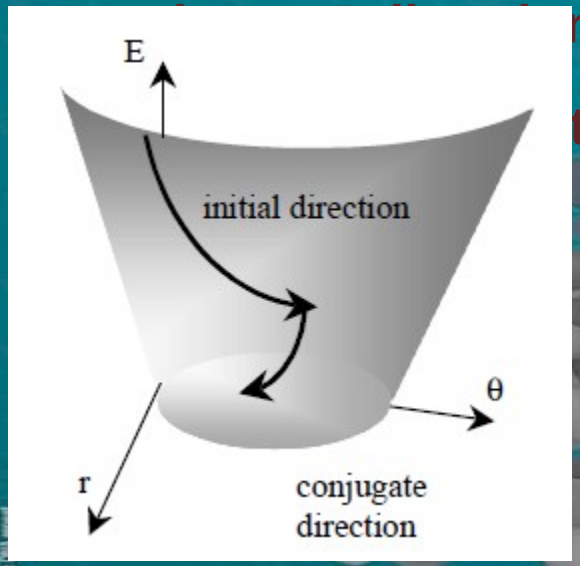


Figure: potential energy surface for the two variables

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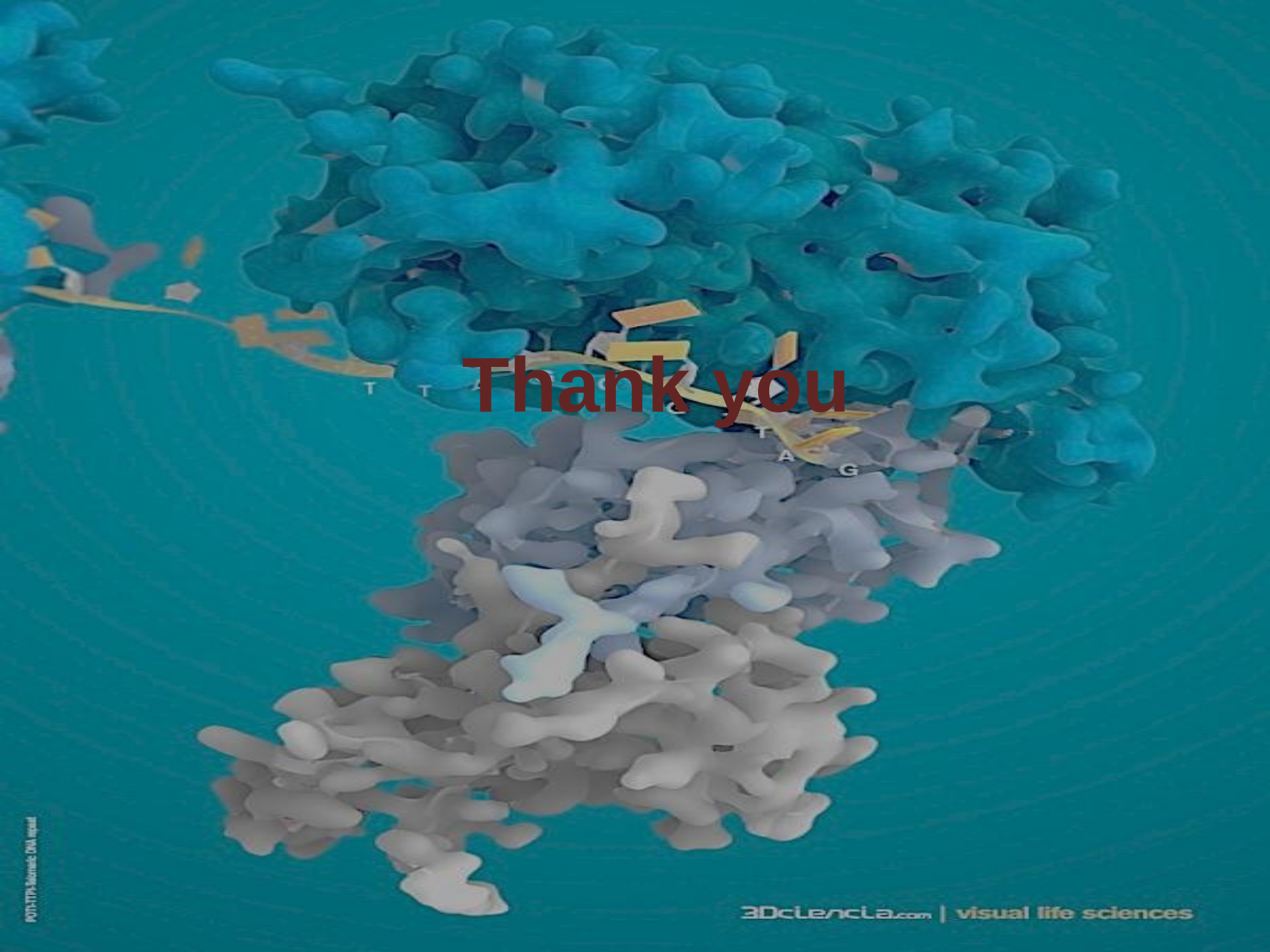
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