# Grading of Problem Set #3: Ligand Binding

Lecture "Interactions of Proteins and Nucleic Acids: Biophysical Concepts and Theoretical Descriptions (BPC2024)"

Winter Term 2024/2025 | Prof. Dr. Karsten Rippe

Web page: <https://malone.bioquant.uni-heidelberg.de/teaching/BPC_lectures/BPC_1+2.html>

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## Grading Rubric (per question)

**Note**: The distribution of the maximum point value per question part is given below. Full points can be awarded despite solutions not being perfect.

**11.0-12.0: Excellent**

* Complete, correct methodology
* Clear reasoning
* Independent analysis demonstrated
* Proper units

**8.0-10.75: Very Good**

* Minor gaps or errors
* Good reasoning shown
* Some improvements possible
* Mostly independent work

**5.5-7.75: Good**

* Significant gaps present
* Basic understanding shown
* Major improvements needed
* Partial independence

**3.0-5.25: Fair**

* Major conceptual errors
* Some correct elements
* Substantial revision needed
* Limited independent thought

**0-2.75: Insufficient**

* Missing or minimal correct content
* Major misunderstandings
* No demonstrated understanding
* No independent analysis

**Common Point Deductions**

* Missing units: -0.5 per instance
* Unexplained assumptions: -0.5 per instance
* Calculation errors: -0.25 to -1 depending on impact
* Missing references: -0.5 per required citation
* Unclear reasoning: -1 to -2 per section

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## Distribution of points between question parts for Problem Set #3

### General principles used for Problem Set #3

* Clear understanding of binding equilibria and ligand binding concepts
* Correct analysis and interpretation of experimental data
* Proper application of thermodynamic principles to binding phenomena
* Appropriate use of mathematical models for cooperativity
* Integration of lecture material with biological context
* Please indicate in a comment if unreferenced use of AI tools is suspected

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### Question 1: Antibody-Antigen Binding Analysis (12 points total)

**1a) Data Plot (3 points)**

* 1.5 points: Correct and clear plot of free antigen vs. added antigen
* 1 point: Proper axes, labels, and scaling
* 0.5 points: Appropriate interpretation of the plot features (saturation point, binding transition)

**1b) Binding Site Determination (4 points)**

* 2 points: Correct determination of 2 binding sites per antibody
* 2 points: Clear explanation of the analysis method and reasoning

**1c) Dissociation Constant Estimation (5 points)**

* 2 points: Appropriate estimation approach
* 1.5 points: Recognition of stoichiometric binding conditions
* 1.5 points: Explanation of limitations (experimental conditions, uncertainty sources)

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### Question 2: Lac Repressor Binding Analysis (12 points total)

**2a) O₁ Binding Site Concentration (3 points)**

* 1.5 points: Correct calculation methodology (1.66 nM)
* 1 point: Proper assumptions about E. coli cell volume
* 0.5 points: Correct units and conversion factors

**2b) Lac Repressor Molecules Estimation (5 points)**

* 2 points: Calculation of Kd from ΔG
* 1.5 points: Correct estimation of molecules needed (~21)
* 1.5 points: Clear statement of assumptions (tetramer binding, 1:1 model, saturation criterion)

**2c) Human Cell Comparison (4 points)**

* 2 points: Correct calculation for human nucleus (~10,500 molecules)
* 1 point: Appropriate scaling of volume differences
* 1 point: Discussion of implications (dilution effect)

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### Question 3: Oxygen Binding to Hemoglobin (12 points total)

**3a) Parameters Interpretation and Model Comparison (5 points)**

* 1.5 points: Correct explanation of Hill parameter (αH = 2.8)
* 2 points: Correct explanation of MWC parameters (R, c, KR)
* 1.5 points: Proper comparison of the models (fit parameters, data representation)

**3b) Cooperativity Description (4 points)**

* 1.5 points: Explanation of Hill equation approach to cooperativity
* 1.5 points: Explanation of MWC model approach to cooperativity
* 1 point: Critical comparison of the models' mechanistic insights

**3c) R-State Fraction Calculation (3 points)**

* 1.5 points: Correct calculation methodology for R-state fraction (~20%)
* 1 point: Proper substitution of parameter values
* 0.5 points: Interpretation of the result in context of the T→R transition