TeBaAb: Text-Based Antigen-Conditioned Antibody Redesign via Directed Evolution

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Abstract

The design of antibodies with high affinity and specificity for target antigens is a cornerstone of therapeutic and diagnostic innovation. Traditional optimization strategies, such as phage or yeast display and directed evolution, remain resource-intensive and limited in their ability to integrate contextual information. Recent AI-driven approaches have accelerated protein engineering, but most rely exclusively on structured inputs, overlooking the potential of natural language as a flexible design interface. In this work, we introduce **TeBaAb**, a novel text-based antigen-conditioned framework for antibody redesign that combines generative modeling with iterative optimization inspired by directed evolution. TeBaAb integrates a Conditional Variational Autoencoder (CVAE) jointly conditioned on antigen sequences and textual descriptions of antibody properties, coupled with a two-stage binding affinity predictor and an iterative enrichment loop. To support this approach, we curated AbDes, a new dataset of 7,800 text–antibody–antigen pairs with accompanying structural and binding information. In silico experimental evaluations demonstrate that TeBaAb improves the predicted binding affinity by an average of 15.5% compared to the original antibodies, while preserving structural confidence (RMSPE < 1.0Å) and generating sequences that are diverse and novel. By enabling text-conditioned antigen-specific antibody design, TeBaAb provides a promising new paradigm for accelerating therapeutic antibody discovery and expanding the antibody design space beyond traditional methods.

1 Introduction

Antibodies are Y-shaped glycoproteins produced by the adaptive immune system to recognize and neutralize foreign molecules, known as antigens. Each antibody binds with high specificity to a particular epitope on the antigen surface, primarily through its complementarity-determining regions (CDRs), which are hypervariable loops located in the variable domains of the heavy and light chains. This molecular recognition mechanism underlies the pivotal role of antibodies in immune

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defense and has been extensively harnessed in biotechnology and medicine. In particular, monoclonal antibodies have become one of the most successful classes of biopharmaceuticals, enabling targeted therapies for cancer, autoimmune diseases, and infectious pathogens [4]. Given their broad utility and therapeutic value, significant efforts have been devoted to the design and optimization of antibodies with enhanced biophysical and functional properties [11].

Traditional antibody engineering relies heavily on iterative trial-and-error strategies such as phage display, yeast display, and affinity maturation through directed evolution [24]. Although effective, these methods are often laborious, time-consuming, and limited by the diversity of physically screenable libraries. Moreover, they require substantial experimental effort to explore a vast combinatorial sequence space and to optimize multiple properties simultaneously. In recent years, artificial intelligence (AI) has begun to transform the landscape of antibody design by enabling data-driven modeling of sequence–function relationships, generating novel candidates, and predicting biophysical properties such as stability and binding affinity in silico. These advances have opened the door to faster, more scalable and more targeted antibody discovery pipelines that complement or even replace traditional wet-lab screening in early stage development [11].

Despite the success of AI-driven approaches in antibody design, most existing computational methods focus on generating or optimizing antibody sequences conditioned solely on structured inputs, such as antigen sequences or 3D structures. These models typically lack the ability to incorporate flexible, high-level design intents specified by users, such as functional requirements, therapeutic context, or developability constraints, especially when such information is only available in natural language form. This limitation restricts the usability and adaptability of current systems in real-world therapeutic discovery workflows, where expert knowledge is often communicated through free-text annotations or design briefs.

Recently, there has been a growing interest in using natural language as a conditioning modality for protein generation [17]. Text-conditioned design offers a promising path toward more intuitive and controllable protein engineering, allowing users to specify desired properties or functional behaviors directly through human language. Inspired by these advances, we introduce **TeBaAb**, a text-based, antigen-conditioned framework for antibody redesign that allows guided optimization through natural language prompts and directed evolution strategies.

In summary, this work makes the following key contributions:

- We propose a novel framework for antibody design. Our framework integrates two key components: Conditional VAE for antibody generation and an optimization pipeline to achieve a higher binding affinity antibody that is guided by our predictor model.
- Although comprehensive data on antibody-antigen pairs are scarce, we have aggregated data from multiple sources, annotated antibodies, to create AbDes, a uniform dataset for antibody design. The dataset and the source code will be publicly released upon acceptance of the paper.
- Our experiments demonstrate the feasibility of designing antibodies based on descriptions while still targeting specific antigens, opening up a new research direction in the field of antibody discovery.

2 Related work

Text-Guided Protein Design. Recent advances in protein language models (PLMs) have laid the foundation for text-guided protein design by modeling amino acid sequences analogously to natural language. Transformer-based architectures such as ESM [21], ProtTrans [8], and various BERT-based models have been pretrained on large-scale protein databases, capturing complex syntactic and functional patterns in protein sequences. Building on these representations, recent approaches have demonstrated the feasibility of generating or editing proteins from natural language prompts. Pinal [6], a 16B-parameter model trained on 1.7B protein–text pairs, uses a two-stage pipeline to map text to structural motifs and then generate sequences, validated experimentally. ProteinDT [18] introduces a three-stage framework: Contrastive alignment (ProteinCLAP), a facilitator network and a decoder trained in 441K text-protein pairs for zero-shot generation and editing. Other models, such as PAAG [27] and ProDVa [16], target functional domain design, and fragment-based generation, respectively. Large-scale models such as ProGen [19] and ESM-3 [10] enable prompt-guided gener-

ation and prediction of fitness. These works demonstrate the growing potential of natural language as a controllable interface for protein design.

Challenges in Antibody Design. Despite advances in general protein design, direct application to antibody engineering faces unique challenges. Antibodies require precise three-dimensional arrangements in their Complementarity Determining Regions (CDRs) while maintaining structural integrity and minimal immunogenicity, constraints fundamentally different from general proteins. Critical limitations include data scarcity: Although general protein-text datasets contain millions of entries, detailed antibody annotations linking natural language descriptions to binding properties and therapeutic functions remain limited [2, 23]. Additionally, structural constraints in antibody design are exceptionally stringent, as function depends exquisitely on precise CDR conformations. Current text-based models may struggle to capture these antibody-specific constraints, potentially generating non-functional or immunogenic sequences [12]. These challenges highlight the need for antigen-conditioned antibody design frameworks that bridge general text-based capabilities with specialized antibody requirements. Our TeBaAb framework addresses this gap by combining text-based property specification with explicit antigen conditioning and iterative optimization tailored for antibody engineering.

3 Methods

3.1 TeBaAb Framework

Antibody engineering has traditionally relied on slow, resource-intensive experimental screening. TeBaAb reimagines this process, offering a data-driven framework that designs antibodies in silico to improve target binding while preserving the structural features essential for proper folding and function.

The framework follows a coordinated two-phase workflow, as illustrated in Figure 1. First, a Conditional Variational Autoencoder (CVAE) generates candidate antibody sequences that are based on both the antigen sequence and the description of the antibody. This conditioning ensures that the proposed modifications are biologically grounded and remain compatible with the existing scaffold. Once these candidates are generated, the second phase takes over: a two-stage deep learning predictor that estimates their binding affinity. This rapid in-silico evaluation allows us to focus on the most promising variants without immediately committing to costly laboratory tests.

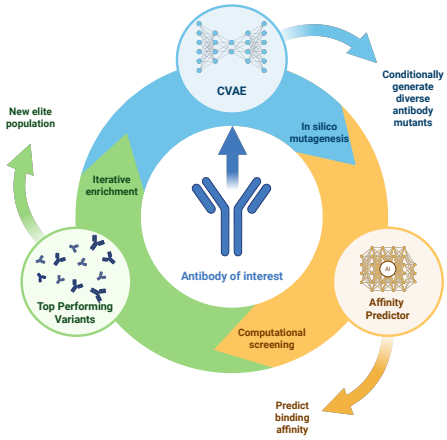

Figure 1: The TeBaAb pipeline integrates generative modeling, predictive evaluation, and iterative refinement for antibody redesign. A Conditional Variational Autoencoder (CVAE) generates candidate sequences conditioned on antigen sequences and textual descriptions. A two-stage affinity predictor evaluates binding strength, and top variants are iteratively fed back into the CVAE, forming an in-silico directed evolution loop. This process yields antibodies with enhanced binding affinity while maintaining structural integrity.

To push the designs further, TeBaAb draws inspiration from directed evolution [25], introducing an iterative loop of generation and selection. In each cycle, the top performing sequence, those with the highest predicted binding affinity, are fed back into the generative process, creating progressively refined variants. Over successive rounds, the population converges toward designs with superior predicted performance, mirroring the efficiency of natural selection, but operating entirely within a computational space.

The result is a self-contained pipeline that replaces slow, resource-heavy screening with a streamlined, model-driven strategy. By weaving together generative modeling, predictive evaluation, and iterative refinement, TeBaAb produces novel antibody sequences that enhance binding capabilities

while honoring the structural constraints required for therapeutic viability. The sections that follow unpack each of these components in detail, showing how they work together to turn a long-standing experimental challenge into a computational design problem.

3.2 Conditional Variational Autoencoder

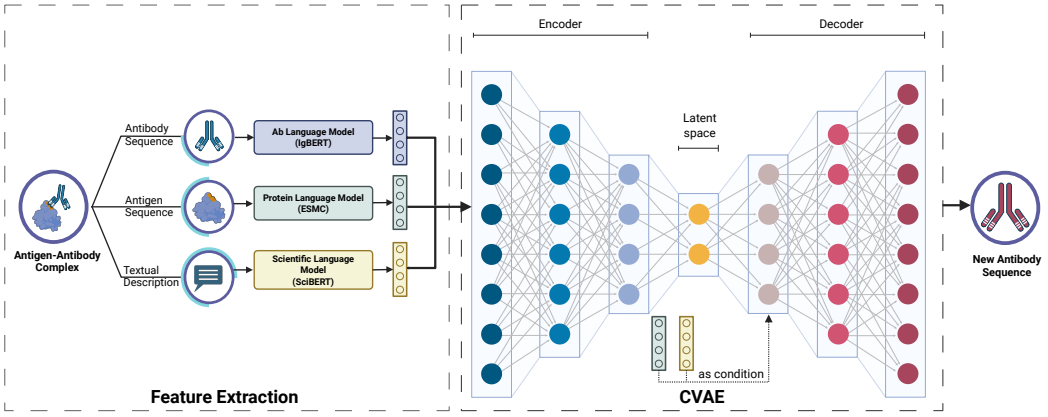

Figure 2: The CVAE integrates antibody embeddings (IgBERT), antigen embeddings (ESMC), and textual description embeddings (SciBERT) to generate antibody sequences. The encoder produces a latent distribution, and the transformer-based decoder reconstructs sequences conditioned on both latent variables and contextual inputs, enabling antigen-specific and text-guided antibody design.

Let the embedding of the antibody be denoted by $\mathbf{x} \in \mathbb{R}^{d_{\text{ab}}}$, representing the encoded representation of the antibody sequence obtained from IgBERT [14], a specialized antibody pre-trained language model. The conditioning vector is defined as: $\mathbf{c} = \left[\mathbf{c}_{\text{antigen}}; \mathbf{c}_{\text{description}}\right]$, where $\mathbf{c}_{\text{antigen}} \in \mathbb{R}^{d_{\text{ag}}}$ represents the antigen embedding extracted using ESMC [10], a protein language model specifically designed to understand protein sequences, and $\mathbf{c}_{\text{description}} \in \mathbb{R}^{d_{\text{des}}}$ denotes the textual description embedding generated by SciBERT [3], a domain-adapted language model for scientific text.

Encoder. The encoder, parameterized by ϕ, takes the concatenated vector $[\mathbf{x}; \mathbf{c}]$ and outputs parameters of the approximate posterior:

$$q_\phi(\mathbf{z} \mid \mathbf{x}, \mathbf{c}) = \mathcal{N}\big(\mathbf{z}; \mu_\phi(\mathbf{x}, \mathbf{c}),\ \text{diag}(\sigma^2_\phi(\mathbf{x}, \mathbf{c}))\big),$$

where μ_ϕ and $\log \sigma^2_\phi$ are learned via neural networks. We then sample the latent representation using the reparameterization trick:

$$\mathbf{z} = \mu_\phi(\mathbf{x}, \mathbf{c}) + \sigma_\phi(\mathbf{x}, \mathbf{c}) \odot \boldsymbol{\epsilon}, \quad \boldsymbol{\epsilon} \sim \mathcal{N}(\mathbf{0}, \mathbf{I}).$$

Decoder. The decoder, implemented as a transformer network parameterized by θ, models the antibody sequence autoregressively conditioned on $\mathbf{z}$ and $\mathbf{c}$:

$$p_\theta(\mathbf{x}_{\text{seq}} \mid \mathbf{z}, \mathbf{c}) = \prod_{i=1}^{L} p_\theta(x_i \mid x_{<i}, \mathbf{z}, \mathbf{c}),$$

where $\mathbf{x}_{\text{seq}} = (x_1, \ldots, x_L)$ denotes the amino acid sequence of length L, with each x_i represented as a one-hot vector.

Objective. The training objective minimizes a weighted sum of the reconstruction loss and the KL divergence loss. This is equivalent to maximizing the Evidence Lower Bound (ELBO):

$$\mathcal{L}_{\text{CVAE}}(\phi, \theta; \mathbf{x}, \mathbf{c}) = \underbrace{-\mathbb{E}_{q_\phi(\mathbf{z}|\mathbf{x},\mathbf{c})}\left[\log p_\theta(\mathbf{x}_{\text{seq}} \mid \mathbf{z}, \mathbf{c})\right]}_{\text{Reconstruction Loss}} + \underbrace{\beta\, D_{\text{KL}}\big(q_\phi(\mathbf{z} \mid \mathbf{x}, \mathbf{c}) \parallel p(\mathbf{z})\big)}_{\text{KL Divergence Loss}},$$

where $p(\mathbf{z}) = \mathcal{N}(\mathbf{0}, \mathbf{I})$ is the prior distribution over the latent space, and β is a dynamically adjusted weight for the KL divergence term, controlled by a proportional-integral (PI) controller [9].

The two components of the loss are:

- **Reconstruction Loss** ($\mathcal{L}_{\text{recon}}$): Implemented as a token-level cross-entropy loss, it measures how well the model reconstructs the input sequence $\mathbf{x}_{\text{seq}}$ given the latent variable $\mathbf{z}$ and conditions $\mathbf{c}$.

$$\mathcal{L}_{\text{recon}} = -\sum_{i=1}^{L} \log p_\theta(x_i \mid x_{<i}, \mathbf{z}, \mathbf{c}),$$

  where L is the sequence length, x_i is the i-th token, and $x_{<i}$ denotes the tokens preceding x_i. Padding tokens are masked (ignored) during loss computation.

- **KL Divergence Loss** (D_{KL}): This term regularizes the latent space by minimizing the Kullback-Leibler divergence between the approximate posterior $q_\phi(\mathbf{z} \mid \mathbf{x}, \mathbf{c})$ (learned by the encoder) and the standard normal prior $p(\mathbf{z})$. This ensures a meaningful and well-structured latent space, facilitating effective sampling for generation.

The PI controller adaptively modulates β during training, encouraging an optimal balance between latent compression (smaller KL divergence) and reconstruction fidelity (lower reconstruction error).

3.3 Binding Affinity Predictor

Inspired by recent advances in protein interaction prediction [22, 13], to predict antibody-antigen binding affinity, we employ a two-stage deep learning framework. For sequence representation, similar to the CVAE model, we use the embedding model IgBERT and ESMC to encode antibody chains and antigens. First, the encoders ϕ_{ab} and ϕ_{ag} are lightweight MLP projectors implemented as single linear layers mapping the pretrained embedding dimensions to a latent space, followed by L2 normalization. We train these projectors *from scratch* with an InfoNCE loss while the pretrained embedding backbones are not fine-tuned. For a batch of N pairs $\{(\mathbf{ab}_i, \mathbf{ag}_i)\}_{i=1}^{N}$, projections are:

$$\mathbf{p}_{\text{ab},i} = \text{normalize}(\phi_{\text{ab}}(\mathbf{ab}_i)),$$
$$\mathbf{p}_{\text{ag},i} = \text{normalize}(\phi_{\text{ag}}(\mathbf{ag}_i)).$$

The contrastive loss is defined as:

$$\mathcal{L}_{\text{cont}} = -\frac{1}{N}\sum_{i=1}^{N} \log\left(\frac{\exp(\mathbf{p}_{\text{ab},i} \cdot \mathbf{p}_{\text{ag},i}/\tau)}{\sum_{j=1}^{N}\exp(\mathbf{p}_{\text{ab},i} \cdot \mathbf{p}_{\text{ag},j}/\tau)}\right).$$

Then, a cross-attention model predicts the binding affinity by capturing their interactions. The affinity predictor, $\mathcal{M}_{\text{aff}}$, uses these encoders and applies multi-head cross-attention as follows:

$$\mathbf{H}_{\text{ab}\to\text{ag}} = \text{MultiHeadAttention}(\mathbf{proj}_{\text{ab}}, \mathbf{proj}_{\text{ag}}, \mathbf{proj}_{\text{ag}}),$$
$$\mathbf{H}_{\text{ag}\to\text{ab}} = \text{MultiHeadAttention}(\mathbf{proj}_{\text{ag}}, \mathbf{proj}_{\text{ab}}, \mathbf{proj}_{\text{ab}}),$$
$$\mathbf{H} = \mathbf{H}_{\text{ab}\to\text{ag}} + \mathbf{H}_{\text{ag}\to\text{ab}}, \quad \hat{y} = \theta(\mathbf{H}).$$

Finally, the loss is the mean squared error defined as:

$$\mathcal{L}_{\text{aff}} = \frac{1}{N}\sum_{i=1}^{N}(\hat{y}_i - y_i)^2.$$

The cross-attention step is necessary because binding affinity is not solely determined by global similarity in the shared latent space. While the contrastive model aligns antibody and antigen embeddings, cross-attention explicitly models conditional interactions between them. This allows the representation of an antibody to be refined with respect to a given antigen, better capturing the pairwise dependencies that underlie molecular binding, and thereby improving the accuracy of affinity prediction.

3.4 Directed Evolution

Our antibody redesign strategy employs a directed evolution approach to iteratively improve antibody sequences towards higher binding affinity. This method mimics natural selection, progressively enriching sequences that exhibit superior fitness. The core idea is to explore the sequence space around an initial set of antibody sequences, evaluate the fitness of newly generated variants, and

then select the most promising ones to serve as the basis for the next generation of exploration. This iterative refinement process aims to converge on sequences with optimal binding characteristics.

The directed evolution process commences by selecting $K = 10$ initial antibody sequences. These sequences are then subjected to an iterative optimization loop spanning $G = 5$ generations. In each generation, for every selected antibody sequence, a set of $B = 20$ neighboring sequences are generated. This generation step is powered by our CVAE. Given an antibody sequence embedding, along with the corresponding antigen embedding ($\mathbf{c}_{\text{antigen}}$) and a desired property embedding ($\mathbf{c}_{\text{description}}$), CVAE samples novel antibody sequences, yet contextually relevant. This allows for exploration of the sequence space while maintaining desired characteristics.

The fitness of these newly generated sequences is then rigorously evaluated. For this, we utilize our pre-trained Binding Affinity Predictor. This predictor acts as a computational oracle, providing an estimated binding affinity ($\hat{y}$) for each antibody-antigen pair. A higher predicted binding affinity (for example, a more negative value of ΔG) signifies a stronger binding interaction, thus indicating a higher fitness. The selection criterion for advancing sequences to the next generation is based on these predicted affinity values. Specifically, the top K antibody sequences, exhibiting the most favorable (highest) predicted binding affinities, are chosen from the combined pool of parent and newly generated sequences to propagate to the subsequent generation. This ensures that the population progressively shifts towards higher-affinity regions of the sequence space.

The fitness score $F(S, A)$ for an antibody sequence S against a target antigen A is directly defined by its predicted binding affinity ($\hat{y}(S, A)$) calculated using our binding affinity predictor $F(S, A) = \hat{y}(S, A)$, where S represents the antibody sequence being evaluated and A represents the target antigen sequence. The objective of the directed evolution process is to minimize $F(S, A)$, thus identifying antibody sequences with the strongest predicted binding affinity to the specific target antigen.

4 Experiments

4.1 Dataset

The development of novel antibody design methodologies, particularly those leveraging text-based conditioning, necessitates a comprehensive and multi-modal dataset. Although existing resources such as the Structured Antibody Database (SAbDab) [7], the AbSet dataset [2], and the AntiBody Sequence Database (ABSD) [20] provide extensive collections of antibody-antigen structures and sequences, a notable gap persists in unifying these with rich descriptive textual annotations. Specifically, to train our proposed text-based antigen-conditioned framework for antibody redesign with a CVAE, a dataset comprising complete antibody heavy and light chain sequences, corresponding antigen information, and contextual textual descriptions for each antibody was essential.

To address this critical data scarcity, we curated a novel dataset, termed AbDes (Antibody Description Dataset). Our construction methodology began with using the AbSet dataset as a foundational source, which provides a meticulously compiled collection of antibody structures and molecular descriptors, often including paired heavy and light chains alongside antigen information and associated Protein Data Bank (PDB) IDs [5]. From AbSet, we meticulously filtered and selected 7,800 complete data pairs, each comprising the heavy chain, light chain, and antigen of an antibody-antigen complex.

A unique aspect of AbDes lies in its integration of descriptive textual information. Utilizing the PDB IDs associated with each filtered entry, we systematically collected additional metadata and textual annotations from the PDB. This collected information includes, but is not limited to, experimental details, source organism, resolution, classification, and other relevant biological and experimental contexts available within the PDB entry files (e.g., from fields like title, classification, organism, expression system, etc.). The entry example can be found in Table 5.

To train the binding affinity predictor module in TeBaAb, we rely on experimentally determined binding affinity measurements, specifically the values of **change in free energy** (ΔG), obtained from SAbDab. Comprehensive entries that included the complete heavy chain, the light chain, the antigen, and an exact value ΔG were relatively scarce. At the time of this study, SAbDab contained only about 400 such unique records, highlighting the persistent challenge of collecting large-scale experimental affinity datasets for machine learning purposes. However, these high-quality measure-

ments formed an essential foundation for developing a predictor capable of estimating the binding strength, an important metric for assessing the performance of the redesign.

4.2 Results

In this section, we present a comprehensive evaluation of the TeBaAb framework, demonstrating its efficacy in the redesign of antibody sequences. As our method introduces a novel approach for text-conditioned antibody design, direct baseline comparisons with existing methods are not feasible. Therefore, we focus on showcasing the performance of TeBaAb across the key evaluation metrics outlined in Appendix A: **Maximum Binding Affinity (MBA), diversity, novelty, and structural confidence**.

4.2.1 Binding Affinity Optimization

Our primary objective is to enhance the binding affinity of antibodies to antigens. Table 1 summarizes the average predicted binding affinity for the original antibodies and their corresponding TeBaAb optimized variants. We report the predicted ΔG values, where lower values indicate stronger binding. The improvement in binding affinity is evident from the decrease in ΔG for optimized sequences.

Table 1: Average Predicted Binding Affinity (ΔG) for Original vs. TeBaAb-Optimized Antibodies.

Metric	**Original** ΔG (kJ/mol)	**Optimized** ΔG (kJ/mol)	**Improvement (%)**
Binding affinity	-10.04 $\pm$ 0.13	-11.60 $\pm$ 0.14	15.5

Note: Improvement (%) is calculated as $(|\text{Optimized } \Delta G| - |\text{Original } \Delta G|)/|\text{Original } \Delta G| \times 100$, reflecting the increase in absolute affinity.

As shown in Figure 3, TeBaAb consistently generates antibody sequences with improved predicted binding affinities, highlighting the framework's ability to effectively optimize this critical property.

4.2.2 Sequence Diversity and Novelty

To evaluate the generative capabilities of TeBaAb beyond affinity optimization, we evaluated the diversity and novelty of the antibody sequences generated. Diversity quantifies the variation within the redesigned set, while novelty measures their distinctiveness from the training data. Table 2 presents these metrics.

Table 2: Sequence Diversity and Novelty of TeBaAb-Generated Antibodies.

Metric	**Value**
Average Levenshtein Distance (Diversity)	87.73
Average Minimum Levenshtein Distance to Training Set (Novelty)	28.95

Note: Higher values for both metrics indicate greater diversity and novelty, respectively.

We adopted the Levenshtein distance [15] as a measure of sequence dissimilarity, as it directly captures the minimal number of insertions, deletions, or substitutions required to transform one sequence into another. This alignment-free metric is widely used in bioinformatics for characterizing sequence similarity, and is well-suited for antibody analysis where small changes in amino acid composition can result in significant functional differences. The calculated average Levenshtein distance indicates that TeBaAb is capable of producing a diverse set of antibody sequences, which is crucial for exploring a

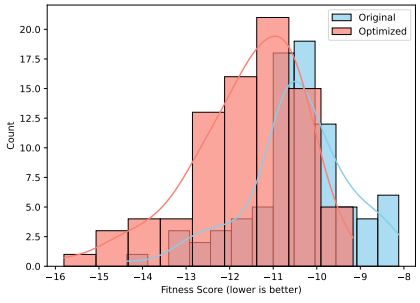

Figure 3: Histogram & KDE: Original vs Optimized Binding Affinity.

wide range of potential solutions. Furthermore, the average minimum Levenshtein distance to the training set of 28.95 demonstrates the framework's ability to generate novel sequences, minimizing overlap with existing data and potentially leading to innovative designs.

4.2.3 Structural Confidence

The maintenance of the structural integrity of the antibody scaffold is paramount for its stability and function. We use ABodyBuilder2 [1] to forecast the three-dimensional configurations of modified antibody sequences, utilizing its ensemble of four models to assess the reliability of the predictions. In Table 3, we report the root mean prediction error (RMSPE) for different regions of the antibody. While the prediction errors of TeBaAb sequences are consistently slightly higher than those of the original antibodies, all values remain below 1.0 Å, a threshold generally considered to indicate high-confidence structural predictions. This suggests that, although sequence modifications introduce minor variability, the optimized antibodies maintain structural characteristics that are well captured by standard prediction tools, supporting their feasibility and stability.

Table 3: Average Structural Confidence (RMSPE) for TeBaAb-Optimized Antibodies.

Region	**Original Pred. Error (Å)**	**Optimized Pred. Error (Å)**
Framework H-chain	0.315 ± 0.013	0.362 ± 0.011
CDR-H1	0.303 ± 0.010	0.290 ± 0.009
CDR-H2	0.190 ± 0.007	0.191 ± 0.005
CDR-H3	0.188 ± 0.005	0.196 ± 0.006
Framework L-chain	0.238 ± 0.006	0.260 ± 0.011
CDR-L1	0.252 ± 0.009	0.307 ± 0.020
CDR-L2	0.182 ± 0.007	0.192 ± 0.008
CDR-L3	0.235 ± 0.007	0.238 ± 0.010
Average	0.238 ± 0.008	0.255 ± 0.010

5 Discussion

The TeBaAb framework represents a significant advancement in computational antibody design, introducing a novel text-conditioned approach to enhance binding affinity while preserving structural integrity. Our results confirm TeBaAb's ability to achieve substantial improvements in predicted binding affinity ΔG, demonstrating its effectiveness in navigating the sequence landscape guided by textual cues. Crucially, this optimization is achieved without compromising the fundamental antibody scaffold, as evidenced by low and consistent structural prediction errors. Beyond affinity, TeBaAb also showcases strong generative capabilities, producing diverse and novel antibody sequences. This capacity to explore a broad and innovative sequence space is vital for identifying unique therapeutic candidates and expanding the antibody repertoire. The development of the AbDes dataset, a comprehensive resource of text-antibody-antigen pairs, underpins this text-conditioned design, addressing critical data scarcity in the field.

Despite these promising outcomes, the current iteration of TeBaAb has limitations. Our evaluations are based on computational predictions, which requires future empirical wet lab validation to confirm functional efficacy. Furthermore, while focused on affinity, the framework's textual conditioning could be expanded to encompass a wider range of developability properties. Future work will prioritize experimental validation, broaden the scope of multi-objective optimization, and explore more computationally efficient design strategies to realize TeBaAb's full potential in accelerating antibody discovery.

6 Conclusion

The development of high-affinity antibodies is a cornerstone of modern medicine, but traditional design methods are often protracted and lack the capacity to integrate nuanced contextual information. In this paper, we introduce TeBaAb, a novel text-based antigen-conditioned framework for

antibody redesign, aimed at overcoming these limitations by leveraging textual descriptions and a robust optimization pipeline. Our work makes several significant contributions to the field of antibody design. First, we proposed a unique framework that integrates a CVAE for antibody generation with an Oracle-guided optimization pipeline, specifically engineered to achieve enhanced binding affinity. Second, recognizing the scarcity of comprehensive antibody-antigen interaction data, we diligently compiled and annotated AbDes, a substantial dataset of 7,800 text-antibody-antigen pairs, which serves as a crucial resource for training text-conditioned antibody design models. Finally, our rigorous in silico experimental evaluations unequivocally demonstrated the feasibility and efficacy of TeBaAb. We showed that our framework consistently generated optimized antibody sequences that exhibited superior affinity binding to target antigens, critically, while maintaining high structural confidence in the predicted structures of the redesigned antibodies. These results underscore TeBaAb's capacity not only to enhance desired properties but also to preserve the structural integrity vital for therapeutic applications.

By enabling the design of antibodies based on descriptive text while ensuring antigen specificity, TeBaAb opens a promising new research direction in antibody discovery. This approach has the potential to significantly streamline the design process, accelerate therapeutic development, and facilitate the creation of next-generation biologics with tailored properties. Future work will explore expanding textual conditioning to encompass a broader range of antibody properties, integrating more complex structural constraints, and validating TeBaAb designs through experimental wet-lab assays.

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A Appendix

A.1 Decoder model

The decoder is built on a Transformer architecture [26] and serves as the core module for generating antibody sequences (see Fig. 4). In the figure, special tokens are also used: **CLS** marks the start of a sequence, **SEP** separates the heavy and light chains, and **EOS** denotes the end of a sequence to ensure proper sequence length. It reconstructs sequences from a rich, combined representation that merges latent features, descriptive metadata, and antigen-specific embeddings. These inputs are concatenated and projected into a sequence of hidden states, forming the "memory" for cross-attention.

During generation, the target tokens are first embedded and enriched with positional encodings, then passed through a stack of Transformer decoder layers. Within each layer, self-attention captures dependencies within the generated sequence so far, while cross-attention draws on the memory to integrate contextual information from the input.

Training employs teacher forcing, periodically replacing predicted tokens with their ground-truth counterparts at a fixed probability to stabilize learning. When teacher forcing is not applied, the decoder generates tokens sequentially using greedy decoding. Finally, hidden states are projected onto vocabulary logits, enabling step-by-step prediction of the next amino acid in the sequence.

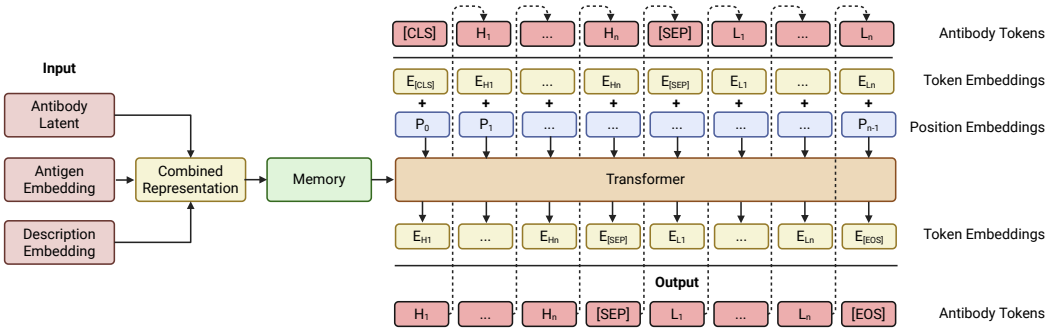

Figure 4: This figure illustrates the design of Transformer-based decoder for antibody sequence generation. The decoder integrates latent features, antigen embeddings, and textual description embeddings into a shared representation that serves as memory for cross-attention. Antibody sequences are reconstructed autoregressively: input tokens (heavy and light chains) are embedded with positional encodings, processed through Transformer layers, and predicted step by step. Self-attention captures dependencies within the sequence, while cross-attention injects contextual information, enabling controllable generation of antibody sequences aligned with antigen specificity and descriptive properties.

A.2 Evaluation metrics

To comprehensively assess the performance of our antibody redesign framework, we employ four primary evaluation metrics: maximum binding affinity (MBA), sequence diversity, novelty, and structural confidence.

Maximum Binding Affinity (MBA). The MBA metric quantifies the highest predicted binding affinity between the redesigned antibody and its specific antigen, reflecting the functional efficacy of the generated sequences. We use the free-energy-change scoring function to estimate MBA. Formally, MBA is defined as:

$$\text{MBA} = \max_{s \in S} \{-\Delta G(s, a)\}, \tag{1}$$

where S represents the set of redesigned antibody sequences, s denotes a single antibody sequence, and a denotes the target antigen. A lower predicted free energy (ΔG) indicates a higher binding affinity.

Diversity. To ensure the generation of varied antibody sequences rather than mere repetitions or minor modifications of known sequences, we measure diversity within the set of redesigned antibodies. Sequence diversity is computed using the pairwise Levenshtein distance [15] averaged over all pairs of generated sequences, formally represented as:

$$\text{Diversity} = \frac{2}{N(N-1)} \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} \text{Lev}(s_i, s_j), \tag{2}$$

where N is the number of antibody sequences and $\text{Lev}(s_i, s_j)$ denotes the Levenshtein distance between two antibody sequences s_i and s_j.

Novelty. Novelty assesses the degree to which the antibodies generated differ from known sequences in our training dataset. We calculate novelty as the average minimum sequence distance between each generated antibody sequence and all sequences in the training dataset ($\mathcal{D}_{train}$). The novelty score is defined as:

$$\text{Novelty} = \frac{1}{|S|} \sum_{s \in S} \min_{s' \in \mathcal{D}_{train}} \text{Lev}(s, s'). \tag{3}$$

Higher novelty scores indicate more distinctive and potentially innovative antibody sequences.

Structural Confidence. Assessing the structural quality of the redesigned antibodies is critical to ensure stability and functionality. We used ABodyBuilder2 [1] to predict the three-dimensional structures of redesigned antibody sequences, leveraging its ensemble of four models to estimate the reliability of the prediction. The root mean squared predicted error (RMSPE) (Å), derived from the diversity among these predictions, serves as a structure-related metric:

$$\text{RMSPE} = \sqrt{\frac{1}{N} \sum_{i=1}^{N} \text{Var}(\mathbf{x}_i)}, \tag{4}$$

where N is the number of residues, and $\text{Var}(\mathbf{x}_i)$ represents the variance in the predicted coordinates of residue i in the ensemble. Lower RMSPE values indicate greater confidence in the predicted structure, ensuring structural reliability for redesigned antibodies without requiring a reference scaffold.

A.3 Additional Results: Impact of Textual Description

This section presents an additional evaluation designed to specifically highlight the contribution of the textual description input to the performance of the TeBaAb framework. Although our primary evaluation focuses on the full TeBaAb model (which incorporates textual descriptions), understanding the isolated impact of this novel conditioning is crucial. To achieve this, we compare the performance of our best performing TeBaAb configuration (with input of textual description) against a variant of TeBaAb where the textual description component ('des_rep') is excluded during both training and inference. This allows us to isolate the specific benefits conferred by conditioning the generation on textual properties.

All other hyperparameters and training procedures remained consistent with the TeBaAb model that performs the best described in Section 4. This ensures a direct comparison of the impact of the description input. Table 4 presents a comparative overview of key evaluation metrics: Binding Affinity, Sequence Diversity, Novelty, and Structural Confidence, between the full TeBaAb framework and its variant without textual description input.

A.4 AbDes Dataset

In this appendix, we provide example entries from the AbDes dataset to illustrate its structure and the type of information it contains. The dataset is designed to facilitate text-conditioned antibody design by linking antibody sequences and their target antigens with rich textual descriptions of antibody properties.

The AbDes dataset comprises entries with the following key fields:

Table 4: Comparative Performance: TeBaAb (with Description) vs. TeBaAb (without Description).

Metric	**TeBaAb (w Description)**	**TeBaAb (w/o Description)**
Binding Affinity Improvement (Avg ΔG %)	15.5	8.9
Diversity	87.73	86.70
Novelty	28.95	26.11
Average Optimized Pred. Error (Å)	0.255	0.282

- **Antibody Sequence**: The complete heavy- and light-chain amino acid sequences of the antibody (e.g. '$heavy\_chain|light\_chain$').
- **Antigen Sequence**: The target antigen to which the antibody binds. Following [7], we use '$/$' to separate different antigen fragments.
- **Description**: A free-text description of the antibody's properties. This field represents our unique contribution, derived from PDB annotations and literature.
- ΔG **(Binding Affinity)**: The predicted binding free energy, where available. This value indicates the strength of the antibody-antigen interaction (lower values signify stronger binding). Note that ΔG values are available for a subset of the dataset.

Table 5: Example Entries from the AbDes Dataset (General Structure).

Antibody Sequence	**Antigen**	**Description**	**Binding Affinity**
$QVQLV...\|QSALT...$	$VVKFMDVY...$	Vascular endothelial growth factor in complex with a neutralizing antibody, classified as an immune system, derived from mus musculus and expressed in escherichia coli, forms a Hetero 6-mer with Cyclic - C2 symmetry.	-11.55
$QVQLQ...\|QVQLQ...$	$KVFGRCEL...$	Hen egg white lysozyme, d18a mutant, in complex with mouse monoclonal antibody d1.3, classified as a complex (immunoglobulin/hydrolase), derived from mus musculus and expressed in escherichia coli, forms a Hetero 3-mer with Asymmetric - C1 symmetry, and has pseudo-symmetry of Asymmetric - C1 with Hetero 3-mer stoichiometry.	-10.45
$QIQLVQ...\|DIVMT...$	$IRDFNNLT...$	Refined crystal structure of the influenza virus n9 neuraminidase-nc41 fab complex, classified as a hydrolase(o-glycosyl), derived from influenza a virus (a/tern/australia/g70c/1975(h11n9)), forms a Hetero 12-mer with Cyclic - C4 symmetry.	-11.02

Note: Sequences are truncated for brevity.