COMPUTATIONAL DESIGN

1 **RFDiffusion**
scaffold generation

2 **ProteinMPNN**
sequence design

3 **AlphaFold 3**
structure prediction

4 **QC Filter**
iPTM / pLDDT / PAE

Attention-guided redesign

structures

ML ANALYSIS

11 **Score-Value Attention Model**

9 **AF3 Predicted Complex**

10 **Feature Matrix**
n residues × 35 features

extract per-residue features

residues

$\mathbf{x}$

α *(attention weights)*

Score Network
MLP: 35 → 8 → 1

Softmax / τ
+ entropy loss

Value Network
Linear: 35 → 1

v (scalar contributions)

$\times$ $\alpha \cdot v$ Σ $\hat{y}$

binding prediction

designs

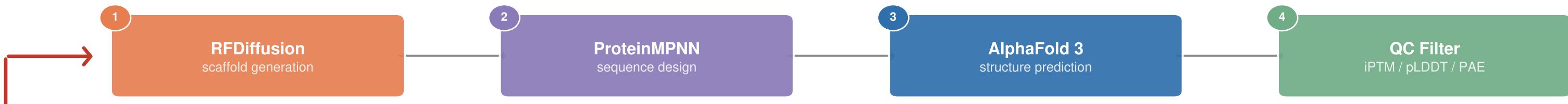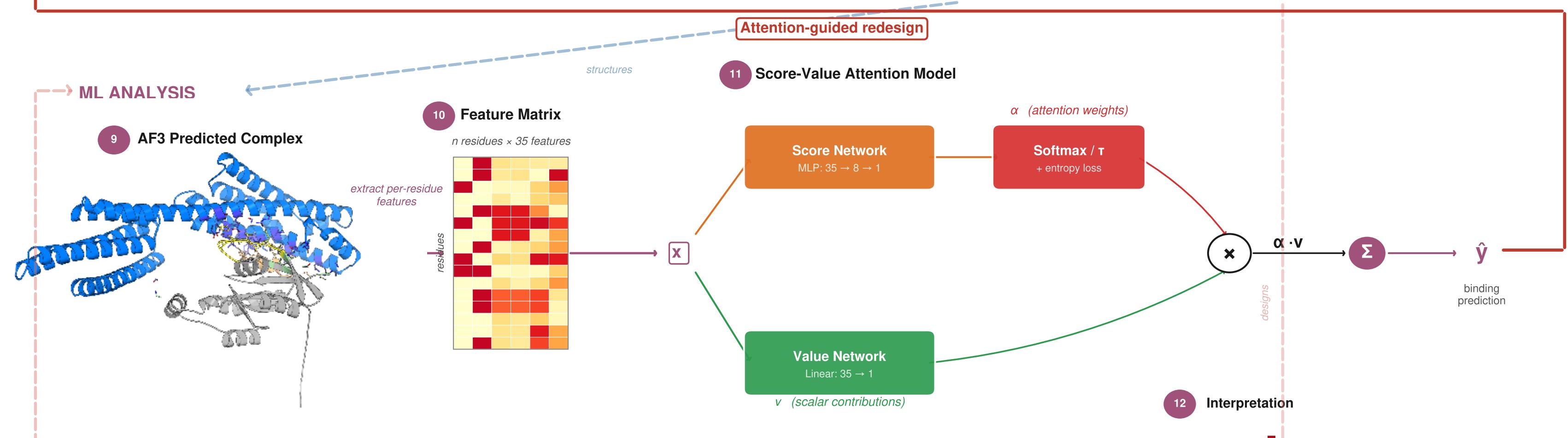**12** **Interpretation**

α

scaffold position

- ■ Inhibitor
- ■ GTPase
- ■ Switch I/II

Scalar values force information through the attention bottleneck → interpretable importance

EXPERIMENTAL VALIDATION

8 **Binding Data**
n = 15 designs

7 **ELISA**
binding assay

6 **Purification**
affinity chrom.

5 **Expression**
E. coli