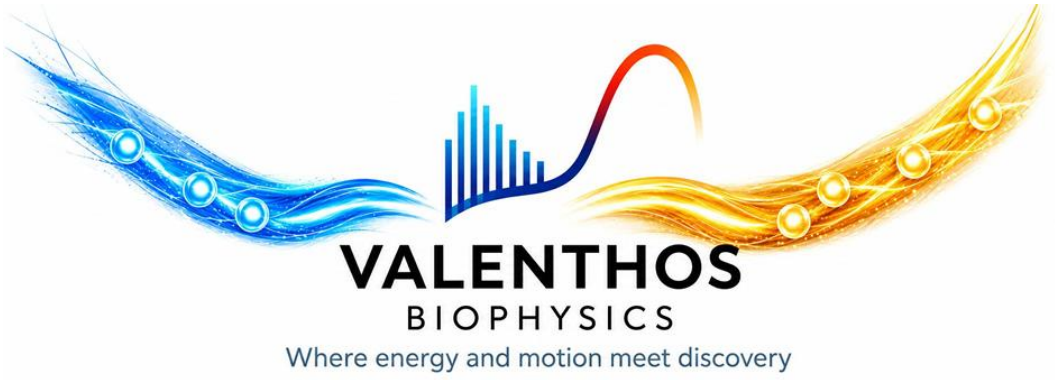

Valenthos Biophysics Manifesto

Drug discovery does not fail because experiments cannot be run. It fails because molecular signals are misunderstood, over-interpreted, or trusted when they should not be.

Valenthos Biophysics exists to address that gap. We operate at the pre-cell, molecular decision layer, where the quality of insight determines everything that follows. Before biology, before chemistry, before scale, there is a moment where a binding event must be understood for what it truly is: signal or artifact, mechanism or coincidence, opportunity or dead end. That moment is where we work.

Valenthos is not a high-throughput CRO and not an assay factory. We do not push buttons or generate data in isolation. We design experiments with intent, integrate orthogonal biophysical evidence, and translate complex molecular behavior into decision-ready understanding. Our work emphasizes protein quality, structural integrity, thermodynamics, and mechanism, because weak assumptions at this stage propagate costly failures downstream.

We believe that every binding event carries information beyond affinity alone: about stability, cooperativity, energetics, and context. When measured with rigor and interpreted with judgment, even weak interactions can reveal viable paths forward. When measured without discipline, they mislead.

Valenthos exists to make that distinction clear. Our engagements are intentionally flexible. We work end-to-end when execution is needed, and we provide independent scientific consulting when it is not. Clients may bring samples, questions, raw data, or partially built platforms. We meet them where they are, but we do not compromise on standards. Our role is not to teach techniques, but to apply expertise to resolve uncertainty. Valenthos maintains strict scope discipline. We focus exclusively on molecular-level biophysics and decision enablement. Cell-based assays, in vivo studies, and medicinal chemistry are outside our execution scope, but not outside our thinking. When structural biology is required, we integrate seamlessly with trusted partners who retain the same scientific leadership and accountability. In an era where speed is often mistaken for progress, we choose clarity. In a field crowded with tools, we prioritize understanding.

Valenthos Biophysics exists for teams who value rigor early, because they know that when biophysics leads, discovery follows.

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Where energy and motion meet discovery

Client Service Portfolio

Our scientific philosophy is translated into the following integrated service areas

01	02	03	04	05	06	07
Target Assessment	**Ligand QC**	**Binding & Kinetics**	**Energetics & Mechanism**	**Screening**	**Assay Development**	**Decision-Grade Integration**
Is the target structurally and functionally suitable for discovery?	*Is my ligand real, clean, soluble, and interpretable in biophysical assays?*	*Does it bind, how strong is the interaction, how fast does it occur?*	*Why does this interaction occur, and what energetically drives it?*	*Which molecules should we move forward with, and why?*	*Can we measure it reliably, robustly, and in the right context?*	*What is the complete picture, and what is the next best step?*

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Structural & Functional Target Assessment

Is This Target Structurally And Functionally Suitable For Discovery?

What we assess:

- ✓ Primary integrity and purity
- ✓ Secondary and tertiary folding state
- ✓ Thermal and chemical stability landscape
- ✓ Aggregation behavior and heterogeneity
- ✓ Quaternary assembly state

Representative platforms: SDS-PAGE, analytical size-exclusion chromatography (aSEC), differential scanning fluorimetry (DSF), circular dichroism (CD; far- and near-UV), intrinsic fluorescence, differential scanning calorimetry (DSC), and dynamic light scattering (DLS).

Deliverables:

- Clear assessment of target structural integrity and folding state
- Stability and aggregation risk profile
- Quaternary assembly characterization
- Explicit recommendation on target readiness for downstream biophysics and discovery

Ligand Quality Control

Is My Ligand Real, Clean, Soluble, And Interpretable In Biophysical Assays?

What we assess

- ✓ Ligand identity and chemical purity
- ✓ Solubility limits and aggregation behavior
- ✓ Concentration accuracy
- ✓ Optical and assay-interfering artifacts
- ✓ prevents false positives downstream

Representative platforms: UV-Vis spectroscopy, plate-based fluorescence controls, DSF interference diagnostics.

Deliverables:

- Ligand purity and solubility assessment
- Identification of aggregation or assay interference risks
- Concentration verification
- Go/no-go guidance for downstream binding and screening studies

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Binding, Affinity & Kinetics

Does It Bind, How Strong Is The Interaction, How Fast Does It Occur?

What we measure

- ✓ Binding affinity (K_D)
- ✓ Association and dissociation kinetics (k_{on}, k_{off})
- ✓ PPI inhibition or enhancement
- ✓ Competitive and allosteric mechanisms
- ✓ Residence time and binding heterogeneity

Representative platforms: *SPR Biacore.*

Deliverables:

- Quantitative binding and kinetic parameters
- Mechanistic interpretation of interaction mode
- Clear conclusions on interaction quality and robustness
- Actionable guidance for optimization or progression

Binding Affinity, Energetics & Mechanism

Why Does This Interaction Occur, And What Energetically Drives It?

What we assess

- ✓ Solution-phase binding affinity independent of surface immobilization
- ✓ Thermodynamic drivers (ΔG, ΔH, ΔS, n & K_D)
- ✓ Coupling between binding and folding or stabilization
- ✓ Stabilizing versus destabilizing ligand effects
- ✓ Orthosteric and Allosteric binders

Representative platforms: Isothermal titration calorimetry (ITC), differential scanning calorimetry (ligand-bound), DSF (quantitative / ThermoMax logic), Dianthus NT.23 TRIC.

Deliverables:

- Solution-phase affinity confirmation
- Thermodynamic breakdown of binding forces
- Insight into binding-coupled conformational effects
- Mechanistic guidance for rational optimization

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Screening Platforms-Biophysics-Driven

Which Molecules Should We Move Forward With, And Why?

What we provide

- ✓ High-information screening of fragments, small molecules, or modulators
- ✓ Rank ordering based on binding, stability, and early mechanism signals
- ✓ Early developability and aggregation flags

Representative platforms: ThermoMax DSF screening, Dianthus NT.23 TRIC screening, plate-based fluorescence assays (Tecan Infinite M1000).

Deliverables:

- Ranked hit lists with biophysical rationale
- Early insight into stabilizing versus destabilizing behavior
- Clear prioritization recommendations for follow-up studies

Tailored Assay Development & Enabling Technologies

Can This Interaction Be Measured Reliably, And Can The Assay Be Built?

What we develop

- ✓ Custom binding and screening assays for challenging targets
- ✓ Target-dependent immobilization and capture strategies
- ✓ Bead-based and surface-engineered systems
- ✓ Enabling assays for phage display and RNA-display
- ✓ Recombinant-protein-specific assay solutions

Representative approaches: Custom bead chemistries, surface functionalization strategies, assay prototyping and validation across SPR, TRIC, and DSF formats.

Deliverables:

- Robust, validated assays tailored to the target and modality
- Documentation of assay performance and limitations
- Enablement of downstream screening and binding programs

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Decision-Grade Analysis & Integrated Deliverables

What Should We Do Next Based On All Available Biophysical Evidence?

What we provide

- ✓ Cross-platform data integration across SPR, ITC, DSC, DSF, TRIC, CD, and QC assays
- ✓ Resolution of conflicting or ambiguous results
- ✓ Mechanistic interpretation grounded in thermodynamics, kinetics, and structural context
- ✓ Explicit prioritization of hypotheses, ligands, and next experiments

Deliverables:

- Decision-focused reports that separate signal from artifact
- Integrated figures and summary tables designed for program-level discussion
- Clear go/no-go/re-design recommendations
- Defined next steps aligned with discovery and optimization goals

Consulting & Scientific Partnership

What Should We Do Next, And How Should The Program Move Forward?

Included but limited to

- ✓ Experimental and biophysical strategy design
- ✓ SPR assay rescue and optimization
- ✓ ITC/DSC/DSF/Thermophoresis/TRIC/QC
- ✓ Program-level interpretation and advisory support
- ✓ Long-term scientific partnership

Deliverables:

- Strategic guidance grounded in biophysical evidence
- Clear recommendations aligned with program goals
- Trusted scientific support throughout discovery and optimization

People & Contacts

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Co-Founder and Scientific Director at Valenthos Biophysics, with expertise in molecular recognition, protein conformational landscapes, and integrated biophysical approaches to drug discovery. He has authored more than 40 peer-reviewed publications spanning protein biophysics, structural biology, molecular chaperones, and drug discovery.

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Co-Founder and Director of Biophysics Development at Valenthos Biophysics, with more than 25 years of biotechnology and biopharmaceutical experience. His background spans biologics and vaccine development, including second-generation Gardasil®, process development, and the integration of biophysical approaches for drug discovery.

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Co-Founder and Director of Operations at Valenthos Biophysics, supporting scientific operations, client engagement, and integrated biophysical programs. He is a co-author of publications on surface plasmon resonance and orthogonal biophysical strategies in fragment-based drug discovery.