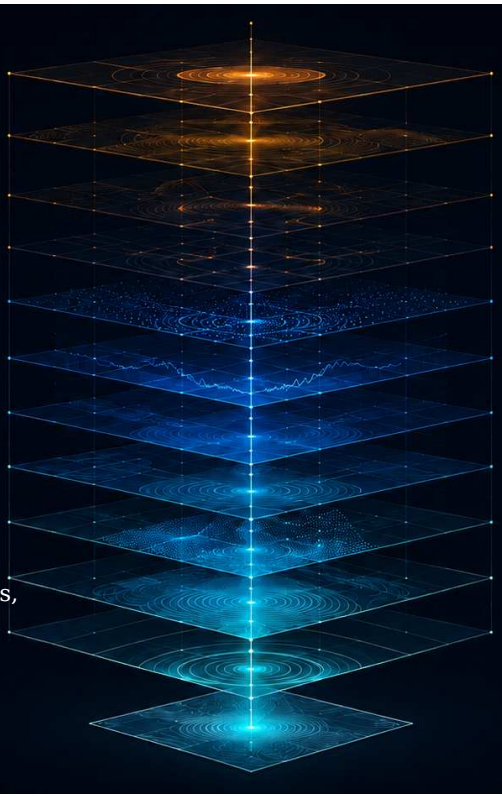
WHITE PAPER 02 / SCIENTIFIC ORIGINS

The Complete Experiment



How Identifyn connected biological intent, controlled methods, acquisition context, native evidence, and scientific decisions - and why preserving that route also protects provenance and intellectual-property boundaries.

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PAPER 02 OF 10
AUGUST 16, 2026

NATIVE EVIDENCE / DETERMINISTIC MEASUREMENT / GOVERNED INTERPRETATION / DEFENSIBLE PUBLICATION

CONTENTS

Paper structure

The complete experiment as the connected scientific object inherited by the BENNETT architecture and the remaining papers in this collection.

All numbered citations link to the corresponding reference. Linked titles in the reference list open the cited source.

ABSTRACT

Paper 1 established why increasingly powerful microscopy could no longer be treated as an isolated act of image acquisition. Higher resolution, larger multidimensional datasets, instrument-specific processing, and expanding analytical choice created a growing burden of evidence. The unresolved question was upstream: what must remain connected before a measurement can be interpreted responsibly?

Identifyn was organized around the answer that the experiment, not the image, is the primary scientific object. A scientific question is translated into biological context, perturbation, sample definition, controls, target and reagent selection, labeling strategy, controlled method, acquisition plan, native instrument record, analysis state, scientific review, presentation state, communication, and a bounded conclusion. Each layer conditions what the next layer can observe, emphasize, interpret, and claim. When these relationships are fragmented, the final image may remain visually compelling while the scientific route that produced it becomes difficult to reconstruct.

This paper defines the complete experiment and explains how Identifyn's vertical integration connected evidence before, during, and after acquisition. The approach does not assume that integration makes a result true. It makes the route inspectable: identities remain addressable, methods remain ordered, deviations remain visible, native evidence remains linked to analytical state, and interpretive, presentation, and communication choices remain linked to what was actually measured. That continuity also preserves the chronology and attribution needed to distinguish published scientific foundations, controlled internal methods, and later inventions. BENNETT inherits this structure as the upstream scientific object on which its governed engines operate.

> Central thesis: Scientific intelligence cannot be reconstructed reliably from an image alone. The observation was conditioned before acquisition, transformed through analysis, and framed through review, presentation, and communication; therefore the complete experiment must remain connected as one evidence-bearing object.

1. Paper 1 left an upstream question

The history described in Paper 1 moved from DNA-repair biology and 4Pi microscopy through advanced fluorescence methods, optical development, instrument integration, Identifyn, and the present BENNETT architecture. The progression exposed a persistent problem: each advance increased not only what could be observed, but also the number of decisions required to make the observation scientifically defensible.

An image is already downstream of many choices. The specimen has been cultured or collected, perturbed, fixed or maintained live, permeabilized when required, blocked, labeled,

washed, mounted, and positioned. Targets and reagents have been selected. Fluorophores have been matched to optical channels. Instrument modality, objective, sampling, detector configuration, Z range, time interval, and acquisition or reconstruction conditions have been chosen. The resulting native record is then subjected to display, measurement, review, and interpretation.

If those choices are not connected, later analysis must infer context from incomplete records. Two files that appear similar may represent different biology, preparation, acquisition, or processing states. Two measurements produced from the same native file may reflect different channels, planes, masks, objects, thresholds, or scientist decisions. A figure may therefore remain intact while the experiment that gives it meaning has fragmented.

The complete-experiment problem begins before the first detected photon and continues through analysis, scientific review, presentation, communication, and the final claim.

2. The experiment, not the image, is the primary object

The most important architectural decision in Identifyn was to organize scientific work around the experiment rather than the image.

An image is one state within a larger system. It is produced by the interaction of biological material, preparation, labeling, optics, sampling, detection, and processing. Its scientific meaning depends on the question asked, the controls used, the perturbation applied, the target measured, and the limitations of the acquisition and analysis route.

The complete experiment therefore contains at least the following connected domains:

1. Scientific purpose: question, hypothesis, disease or pathway context, intended comparison, evidence required, and the limits of what the study is designed to establish.
2. Experimental condition and perturbation: treatment, dose, duration, sequence, environmental condition, comparator, and control state.
3. Sample and specimen state: biological source, cell or tissue system, culture or collection condition, fixation or live-state condition, preparation state, and handling history.
4. Targets, reagents, and labeling system: biological target, epitope when relevant, reagent identity and lot, primary and secondary reagents, concentration or molarity, conjugation state, fluorophore, buffers, mounting media, and controls.
5. Controlled experimental method: the ordered preparation and manipulation process; defined materials and quantitative parameters such as volume, molarity or concentration, duration, and temperature; acceptance criteria; deviations; and responsible operator. Individual operations, including fixation, permeabilization, blocking, washing, labeling, and mounting, remain subordinate parts of that controlled method rather than independent scientific domains.

6. Acquisition and reconstruction context: instrument, modality, objective, detector path, channels, physical sampling, Z or time structure, positions or scenes, and acquisition or reconstruction state.
7. Native evidence record: numeric arrays, axes, physical scale, channel descriptions, instrument metadata, series, coordinate relationships, warnings, and source provenance.
8. Analytical method and state: selected scope, channel roles, background method, thresholds, masks, regions, objects, measurements, exclusions, algorithm or software state, and validation state.
9. Scientific review and interpretation: reviewer selections, comparison criteria, assumptions, alternative explanations, accepted or rejected outputs, uncertainty, interpretive rationale, and downstream consequences.
10. Presentation state: selected images or fields, planes or projections, channel visibility and color, black and white points, gamma or other display mapping, cropping, overlays, annotations, figure assembly, and the explicit separation of display from measurement.
11. Communication and claim formation: intended audience and delivery context, selected evidence, narrative framing, observations, conclusions, limitations, methods, references, and the connection back to every preceding domain.

These are not eleven independent documents. They are eleven responsibilities within one experiment object. The downstream domains are not administrative afterthoughts. Once the data reach scientific review, two qualified reviewers can make different selections, emphasize different regions or comparisons, apply different presentation states, and construct different narratives from the same underlying dataset. Some differences may reflect legitimate scientific questions. Others may reflect expectation, habit, preferred delivery, or confirmation bias. If those choices are not preserved, the route from analysis to communication becomes effectively reviewer-dependent: "dealer's choice" rather than a reproducible scientific state.

BENNETT does not eliminate scientific judgment or claim that interpretation can be made bias-free. It makes the judgment inspectable by preserving what the reviewer selected, how the data were presented, why an interpretation was accepted, which alternatives were considered, and how the intended communication shaped the final claim.

3. Evidence is created before acquisition

Microscopy is often discussed as though the instrument creates the evidence. The instrument creates an acquisition record, but the conditions that determine what can be detected have already been shaped upstream.

Target selection determines which biological relationship is being tested. Reagent specificity and epitope accessibility influence which structures can be labeled. Conjugation and fluorophore behavior affect signal intensity, spectral compatibility, and stability. Fixation and permeabilization affect morphology and access. Blocking, incubation, washing, mounting, and storage can alter signal-to-background and preservation. Controls determine whether an observed fluorescence distribution can be interpreted as specific, nonspecific,

treatment-associated, preparation-associated, or unresolved.

This principle was evident in the methodological work required for super-resolution microscopy. Preparing immunofluorescence samples for more demanding optical systems required attention to labeling density, fluorescence stability, background, three-dimensional preservation, and the relationship between preparation and observable structure. The published methods were not ancillary to imaging; they were part of the measurement system itself.[1]

The same logic later became explicit in Identifyn. Experiment design connected molecular pathway, target selection, antibody and fluorophore compatibility, protocol generation, imaging-system selection, and downstream analysis rather than treating them as unrelated search tasks. The public patent record for Systems for Cellular Experiment Design describes this integrated relationship and lists Brian T. Bennett as inventor and GMD12, LLC as assignee.[2]

The implication is direct: evidence does not begin when a file is uploaded. The uploaded native file carries forward an upstream experimental history that must remain addressable.

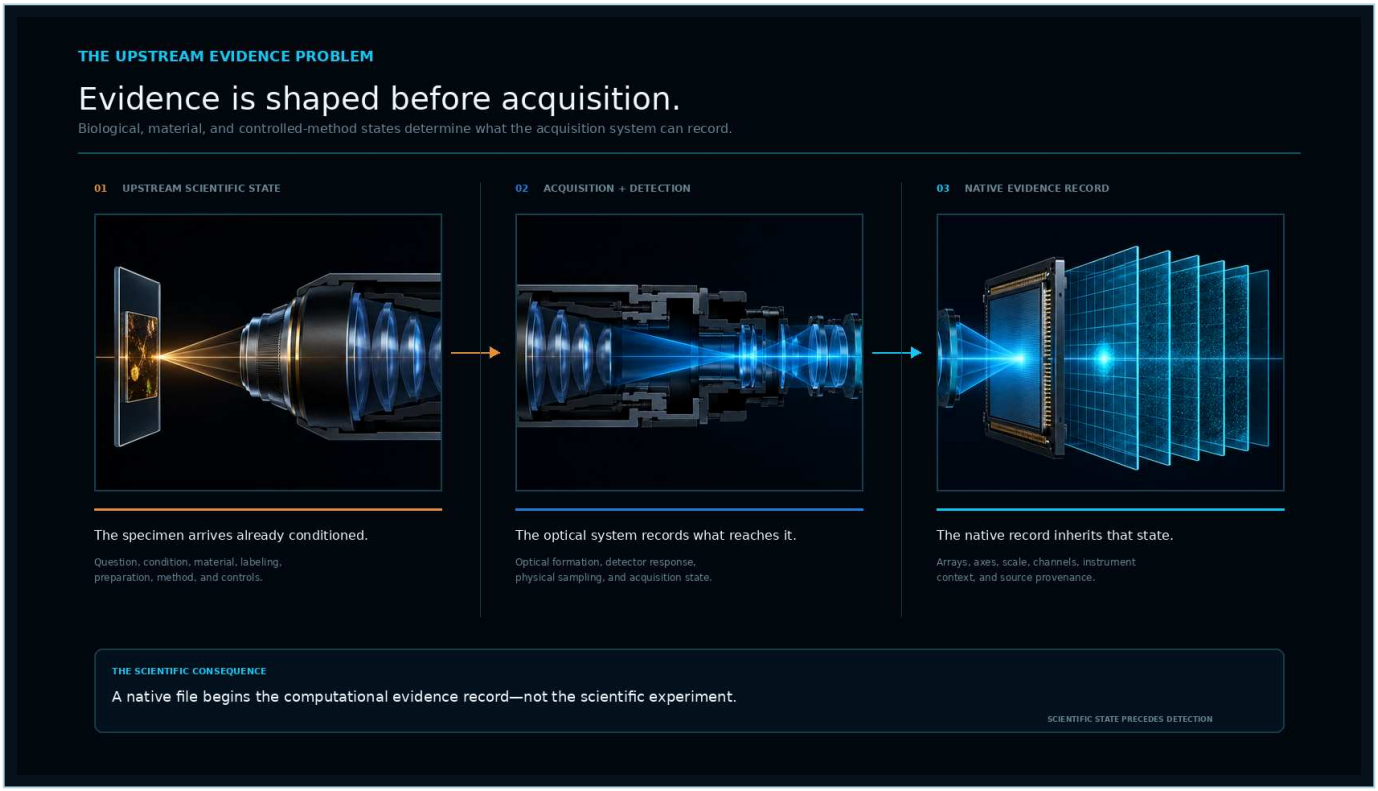

Figure 1. Biological, material, and controlled-method states shape what the acquisition system can detect. The native record begins the computational evidence record, not the scientific experiment.

4. Vertical integration preserves scientific semantics

Vertical integration does not require one organization to manufacture every reagent, own every microscope, or replace every specialist tool. It means that scientific meaning survives the transitions between layers.

A target identifier should remain connected to the reagent used to detect it. The reagent should remain connected to its conjugation or secondary-labeling strategy. The labeling strategy should remain connected to the optical channels and acquisition method. The acquisition method should remain connected to the native arrays and metadata it produced. The arrays should remain connected to the exact analytical state used for measurement. The measurement should remain connected to the observation and conclusion it supports.

The connection must be structural, not rhetorical. Listing a reagent and an instrument in the same report is not sufficient. A vertically integrated record uses identifiers, ordered states, explicit dependencies, and provenance so that a downstream output can be traced to the precise upstream inputs that conditioned it.

This principle aligns with broader efforts to improve scientific reuse and reproducibility. The FAIR principles emphasize that data and associated resources should be findable, accessible, interoperable, and reusable.[3] REMBI defines recommended metadata for biological images so image data can be understood and reused in context.[4] QUAREP-LiMi addresses quality assessment and reproducibility across the light-microscopy workflow.[5] These standards reinforce a common point: pixels alone do not constitute a reusable scientific record.

Identifyn's contribution was to treat these relationships as part of the experimental operating model rather than as documentation added after the fact.

The same structure also protects intellectual continuity. A connected record distinguishes what came from published science, what was established as controlled internal practice, what was changed through later development, and which inventor is associated with the resulting method. It does not, by itself, determine legal ownership or patentability. It preserves the chronology, attribution, dependencies, and evidence needed to prevent later inventions from being detached from the scientific work that produced them.

5. Controlled methods make the route repeatable

The complete experiment requires more than a protocol stored as prose. It requires controlled process.

For a reader unfamiliar with it, Lean, written LEAN in Identifyn's internal operating language, is not an acronym and does not simply mean cutting cost, removing people, or doing more work with fewer resources. Its modern lineage comes from the Toyota Production System. Toyota describes that system through two core ideas: Just-in-Time, which connects work into a coordinated flow, and jidoka, often translated as automation with a human touch, in which work stops when an abnormality is detected so quality can be protected before the error travels downstream.[6] The broader term lean production was subsequently used to describe this operating philosophy outside Toyota and was widely disseminated through the MIT-led research summarized in The Machine That Changed the World and later Lean Thinking.[7]

The simplest scientific translation is this: make the current best-known process visible; distinguish required work from delay, duplication, ambiguity, and rework; detect abnormal states early; preserve who intervened and why; and improve the process from evidence. Standardized work is not a claim that one method will remain correct forever. It documents the present reproducible state, reduces unexplained variation, supports training, and creates a baseline from which an intentional improvement can be measured.[8]

According to the Identifyn founder chronology, LEAN was introduced because the complete experiment crossed too many scientific and operational handoffs to be governed reliably by memory alone. Experiment design, reagent selection, sample preparation, imaging, metadata, analysis, review, and reporting could each be locally correct while still losing meaning between them. Identifyn therefore adapted LEAN from a production philosophy into a scientific evidence discipline: the value stream became the evidence route; standard work became the controlled experimental method; an abnormality became a stop-and-review state; and continuous improvement became a versioned change supported by recorded evidence.

The purpose was not to turn discovery science into an assembly line or eliminate expert judgment. It was to control the repeatable portions of the work so that scientist judgment became visible precisely where biology, measurement, or interpretation required it. This distinction later became important to BENNETT. Prerequisites, ordered states, acceptance gates, exception handling, scientist intervention, and provenance could be encoded because Identifyn had already made the underlying work observable.

A controlled experimental method establishes the expected sequence and records the parameters that can materially affect the specimen and signal: quantities, volumes, molarities or concentrations, incubation times and temperatures, fixation, permeabilization, blocking, washing, mounting, and handling. A scientist may still change a preparation parameter, redefine a region, confine an analytical Z range, reject a mask, select a different projection, or exclude an object. The scientific value is preserved when that intervention becomes an explicit state with a recorded scientist or operator, reason, scope, parameter change, and downstream consequence.

Standard work and scientist judgment are therefore complementary:

- standard work preserves repeatability;
- acceptance criteria expose whether a step is complete;

- deviations preserve what changed and why;
- scientist intervention resolves biological ambiguity;
- provenance connects every action to the resulting evidence state.

This operating discipline preceded BENNETT's formal engine architecture. It supplied the ordered workflows, distinctions, negative paths, and review points that could later be translated into governed computational states. Paper 6 will examine that translation from expert practice to executable scientific intelligence.

6. Handoffs are the primary failure surface

Many experiments do not fail inside a single task. They weaken at the handoffs between tasks.

A product record may identify an antibody but omit lot, clone, conjugation, concentration, or storage state. A method may specify staining but not connect the fluorophores to the acquisition channels. An instrument may preserve rich metadata in the native file while an exported image removes axes, calibration, detector settings, or reconstruction history. Analysis software may generate measurements while the scope and parameters remain in a user's memory. Scientific review may select one subset, comparison, or interpretation without recording the alternatives considered. A figure may preserve the appearance of a result without preserving the display state or the exact measured object set. Communication may then emphasize the evidence most suited to the expected audience or delivery while other relevant evidence becomes less visible.

None of these failures requires misconduct. They emerge when responsibility ends at a local boundary and the next system receives only a partial representation.

The complete experiment treats every handoff as a governed transfer:

Handoff	Minimum state that must survive
Scientific question → experiment design	biological context, intended comparison, controls, permissible claim
Experiment design → materials	target, epitope or binding logic, reagent identity, labeling strategy, compatibility
Materials → method	quantities, order, timing, temperature, handling, deviations
Method → acquisition	sample state, fluorophores, expected channels, modality, sampling requirements
Acquisition → native record	arrays, axes, scale, channels, metadata, processing state, provenance
Native record → analysis	file identity, scope, mappings, parameters, masks, objects, validation state

Handoff	Minimum state that must survive
Analysis → scientific review	measured outputs, eligible comparisons, quality state, exclusions, alternatives, uncertainty
Scientific review → presentation	selected evidence, planes or projections, channels, display mapping, annotations, figure assembly
Presentation → communication	intended audience, delivery context, evidence included or omitted, interpretation, claim, limitations, methods

The strength of the record depends on the continuity of these transfers.

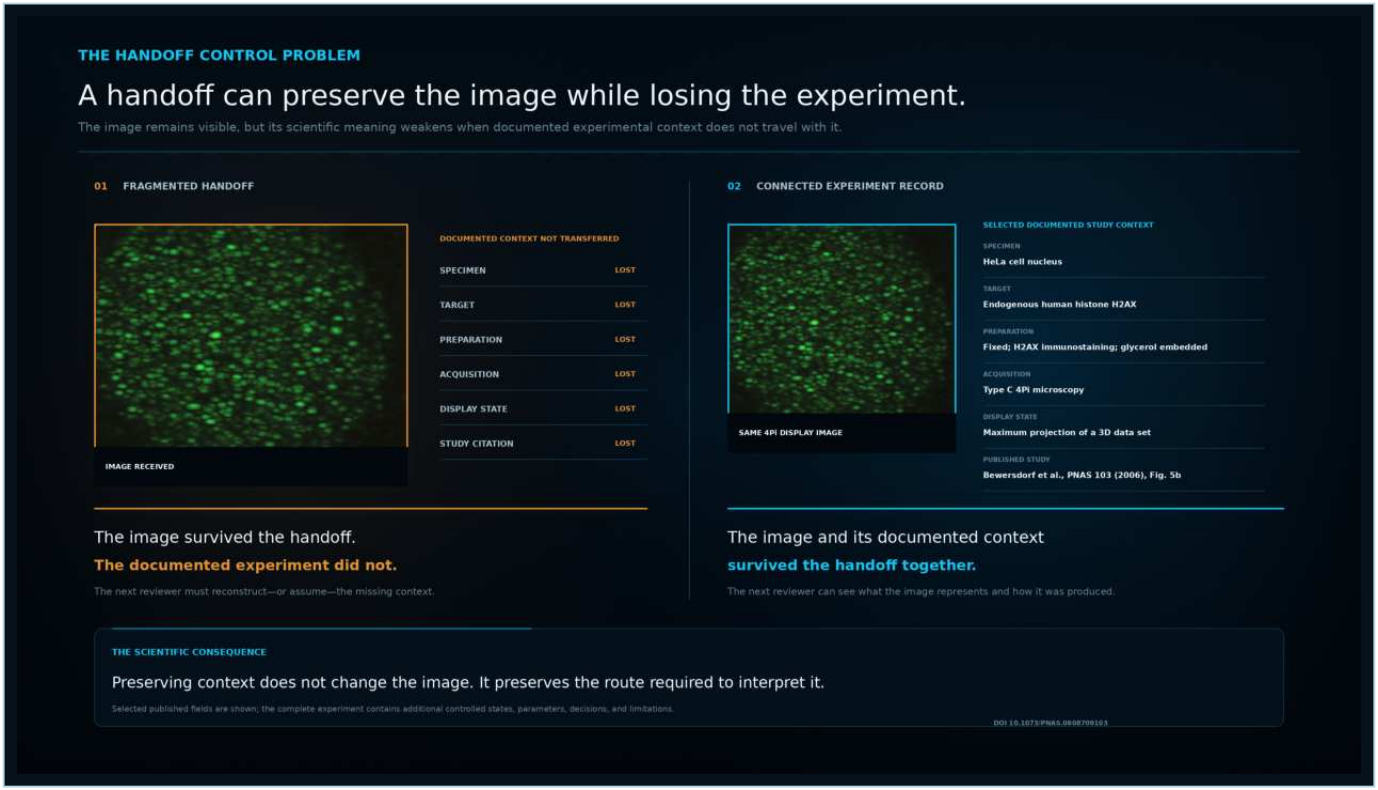

Figure 2. A handoff can preserve an image while losing documented experimental context. Preserving context keeps the route required for responsible interpretation. Source image: Bewersdorf et al., PNAS 103 (2006), Fig. 5b. Copyright © 2006 National Academy of Sciences.

7. The complete experiment is a graph of dependencies

A linear protocol is useful, but the scientific structure of an experiment is a dependency graph.

One biological question may require several perturbations and controls. One sample condition may be evaluated with several targets. One target may be associated with more than one

reagent or labeling route. One acquisition may contain multiple channels, Z planes, timepoints, scenes, or positions. One native record may support several eligible analyses, each with different prerequisites and claim boundaries. One conclusion may depend on several measurements and may remain valid only while all required states are accepted.

Representing the experiment as a graph makes these relationships explicit. Each object has identity and state. Each connection declares what the downstream object inherits. A change upstream can invalidate or require review downstream.

For example:

- changing a target-to-channel assignment requires affected measurements to be recomputed;
- changing an accepted Z range changes the analytical volume but never alters the preserved source stack;
- changing a mask invalidates measurements derived from the earlier mask;
- changing display contrast, gamma, channel visibility, color, projection, crop, or figure selection cannot change quantitative results, but it can materially change what a reviewer perceives and emphasizes;
- changing the interpretive comparison or excluding an alternative explanation creates a new review state that must be justified;
- changing the intended audience or delivery context may change presentation and narrative emphasis, but it cannot rewrite the underlying evidence or erase limitations;
- changing a reagent or preparation creates a different experimental condition rather than silently overwriting the prior one.

This dependency logic is the foundation of governance. It allows the system to know not only what exists, but also what must be reconsidered when a scientific state changes.

8. Integration does not make a result true

The complete experiment is an evidence architecture, not a guarantee of biological truth.

A fully documented experiment can still contain a poor reagent, inadequate control, unsuitable sampling interval, reconstruction artifact, saturated signal, underpowered comparison, or incorrect interpretation. Vertical integration does not remove those risks. It makes them easier to locate, test, and communicate.

The architecture therefore distinguishes among:

- what was planned;
- what was performed;
- what was acquired;
- what was observed;
- what was measured;

- what was interpreted;
- what was presented;
- what was communicated;
- what was validated;
- what remains uncertain; and
- what the evidence does not support.

That separation matters for both scientists and AI systems. A model should not convert a planned method into a completed action, an observed fluorescence distribution into a molecular interaction, a visually emphasized region into a quantitatively dominant result, or an internally validated workflow into independent peer review. The connected record supplies the states required to prevent those category errors.

Interpretive bias cannot be governed by pretending that review is objective or that a figure is a neutral window onto the data. Governance begins by acknowledging that reviewers select, compare, exclude, display, and narrate. The required control is to preserve those choices, their rationale, the alternatives considered, and the evidence that constrains the final claim.

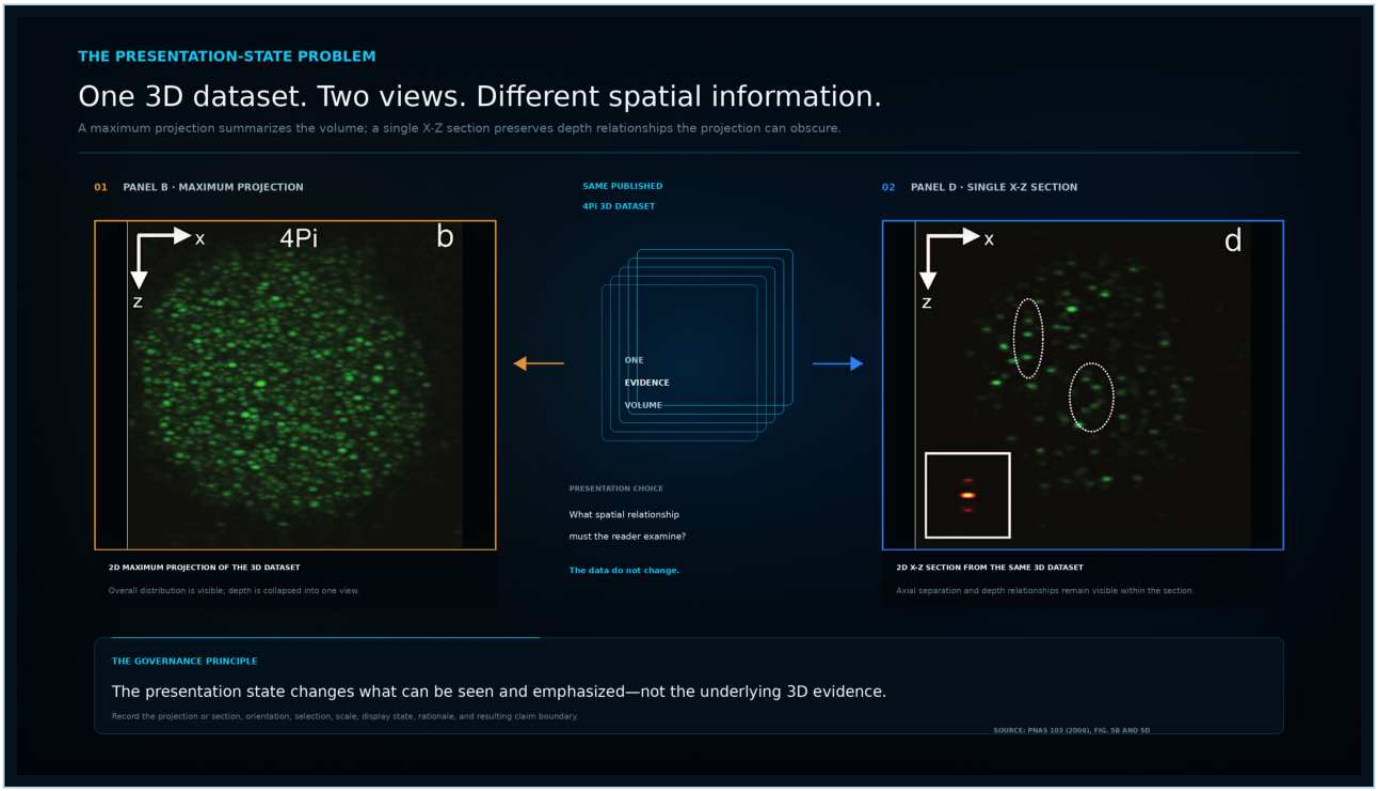

Figure 3. The published 4Pi dataset can be presented as a 2D maximum projection or a single X-Z section. The source evidence remains unchanged, while each view exposes different spatial information. Source: Bewersdorf et al., PNAS 103 (2006), Fig. 5b and 5d. Copyright © 2006 National Academy of Sciences.

9. BENNETT inherits the complete experiment

BENNETT does not begin with a detached image and attempt to reconstruct the experiment through conversation. It inherits the Identifyn principle that the experiment is the primary object and that the native file is the acquisition measurement record within that object.

This upstream structure gives BENNETT a governed starting point. The system can distinguish biological intent from acquisition capability, source evidence from display state, deterministic measurement from interpretation, scientific review from presentation, and scientist intervention from automated operation. It can identify missing prerequisites instead of fabricating them. It can present eligible tools without implying that every file supports every analysis. It can carry methods, parameters, review choices, display states, warnings, exclusions, alternatives, delivery context, and claim boundaries into the final record.

The complete experiment is therefore not background information supplied to BENNETT. It is the scientific structure that makes governed operation possible.

The detailed implementation is developed later in the collection:

- Paper 5 defines the native file as the acquisition GroundTruth™;
- Paper 6 translates expert practice into governed states and routes;
- Paper 7 formalizes scientist-controlled operation;
- Paper 8 defines composable engines and micro-engines;
- Paper 9 defines the Publisher boundary.

Paper 2 establishes what all of those components are responsible for preserving.

10. Why the complete experiment matters

For a scientist, the value is continuity. The result remains connected to the exact biological condition, material state, method, acquisition, analytical scope, review rationale, presentation state, and communication context that produced it.

For a laboratory or imaging core, the value is operational reproducibility. Standard work and expert intervention can coexist without allowing critical decisions to disappear into memory.

For a biotechnology or pharmaceutical organization, the value is comparability. Treatment, dose, time, target, reagent, sample, imaging, measurement, and conclusion can remain addressable across experiments and populations.

For an AI company or technical diligence team, the value is constrained context. The model does not receive an unstructured image and unlimited interpretive authority. It receives a connected scientific object in which states, dependencies, missing prerequisites, measurement authority, and claim boundaries are explicit.

The customer is not merely buying fewer clicks. The customer is buying less loss of scientific meaning.

11. The question and intellectual-property continuity handed to Paper 3

The complete experiment preserves the conditions that produced an observation. It does not yet answer whether that observation remains stable when the same biology is examined through different optical resolutions, sampling regimes, reconstruction methods, or analytical scales.

That question is essential because increased resolution can separate structures that appeared merged, reveal distributions that lower-resolution systems averaged together, and change which measurements or claims are scientifically eligible. Conversely, a feature visible in one optimized modality may not remain supported when examined across other resolutions or evidence tiers.

Paper 3 therefore inherits a complete experimental record and asks:

> Which observations and claims remain stable when the same biology is examined across resolution scales?

That is the role of Resolution Stepdown.

This transition also has an explicit intellectual-property record: U.S. Patent Application No. 19/289,452, Resolution Walkdown Microscopy, invented by Dr. Brian T. Bennett.[12] Paper 3 uses Resolution Stepdown as the explanatory scientific framework for examining what remains visible, measurable, and supportable across changes in resolution and modality. The patent title and the paper title are not interchangeable labels; they occupy different roles within the same documented development history.

That distinction matters. Scientific continuity preserves the evidence route. Intellectual-property continuity preserves how a method emerged from that route, who invented it, and where the later inventive framework is separated from prior publications, institutional work, vendor technology, and third-party contributions. This paper establishes the scientific provenance connecting the complete-experiment framework to the later Resolution Walkdown invention.

Figure 4. Confocal and 4Pi X-Z sections distinguish observations that remain supported from those that depend on resolution. Paper 3 formalizes this Resolution Stepdown question. Source: Bewersdorf et al., PNAS 103 (2006), Fig. 5c and 5d. Copyright © 2006 National Academy of Sciences.

Conclusion

The complete experiment is the unit of scientific intelligence.

Identifyn established that evidence begins with biological intent and controlled materials and methods; passes through sample state, acquisition context, and the native instrument record; and becomes defensible only when analysis, scientific review, presentation, communication, and bounded claim formation remain connected to that upstream history.

This vertical integration does not replace specialist instruments, software, standards, or scientists. It harmonizes them around a common obligation: every meaningful output must remain addressable to the experiment, evidence, decisions, and limitations that produced it. The same traceability protects the distinction between scientific precedent, controlled know-how, and later invention.

BENNETT makes that connected route executable. Paper 3 now tests what happens when the same complete experiment is examined across resolution.

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