Diagnostic Visual Information in the Use of Microscopes in Histology

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Abstract

The science of histology depends on the skilled use of microscopes. Visual cognition in the use of microscopes is sometimes a matter of immediate recognition and very often a matter of extensive exploration and hypothesis testing. In every case, there are fundamental questions about how visual information is used to drive cognition. In an experiment that varied the visual information available to students of histology, nearly any sample of tissue provided access to the part-whole hierarchy and taxonomies learned in the science. How specific the recognition was, depended on the uniqueness of the morphology. The precise manner in which information accumulated for complete recognition of a tissue varied from tissue to tissue.

Keywords: medical imaging; visual cognition; visual search; microscopy; perception; reasoning; scientific reasoning; education.

Visual Information in a Real World Domain

The science of histology is the study of the microanatomy of biological tissue. It is a fundamental biological science and forms the basis for the medical discipline of pathology (e.g., Ross, Kaye, & Pawlina, 2003). Histology is practiced in large part through studying tissues in microscopes. Thus, visuocognitive skill is at the center of mastering a complex scientific domain (e.g., Crowley, Naus, Stewart, & Friedman, 2003; Pani, Chariker, & Fell, 2005; Pani, Chariker, Claudio, & Fell, 2006). This paper reports a part of our effort to understand visuocognitive skill in such an advanced discipline and complex domain.

Use of a microscope very often includes extended exploration of the microscope slide. Magnification is changed often, and the position of the slide under the microscope is systematically manipulated for purposes of exploration (consider also Hoffman, 1984; Kundel, 2000; Kundel, Nodine, & Carmody, 1979; Lesgold, Rubinson, Feltovich, Glaser, Kopfer, & Wang, 1988). One reason for this exploration is that microscopy in histology is quite often very challenging (Crowley et al., 2003; Pani et al., 2005, Pani et al., 2006). The domain of histology is complex, and the use of thin slices sampled from the interior of a tissue, as illustrated in Figure 1, creates many problems for visual recognition.

A useful formulation of the task in microscopy is to consider it to be a visual information system in which there is a target domain of structure, microanatomy in this case, and an information domain of visual structure, here the microscope slides, that is used to gain information about the target domain. It appears to be a particular problem in histology that the mapping from whole tissue in the target domain to the thin microscope sections in the information domain is for many individual structures both one to many and many to one (see Pani et al., 2005). As a consequence of this challenging mapping between domains, hypothesis testing becomes a fundamental part of the practice of microscopy.

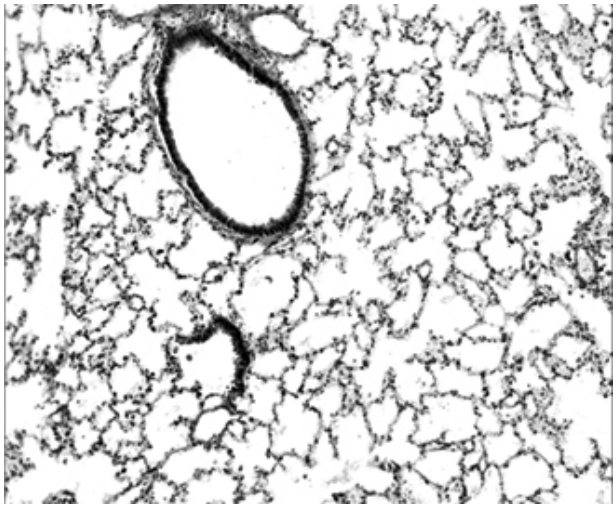

Figure 1. Air passages and air sacs from the lung viewed through a standard light microscope.

An understanding of visuocognitive skill in microscopy requires knowing how practitioners use visual information in the slides to recognize tissues (consider also Oliva & Schyns, 1997; Schyns, Goldstone, & Thibault, 1998). For example, and in the simplest terms, what information in the slides permits immediate recognition? Perhaps more importantly, when partial recognition drives hypothesis testing and exploration, what visual information is recognized, and what is the character of the knowledge that is activated?

A pursuit of these questions requires a specific formulation of the mapping between target and information domains in histological microscopy. Systematic naturalistic studies have provided a good starting point for this (Crowley et al, 2003; Pani et al., 2005). In the target domain of microanatomy, there are several well established taxonomies. For example, there is a well articulated taxonomy of glandular structures. We have found, however, that taxonomies are not the primary basis for discourse when practicing microscopy. The major organization of knowledge is in terms of part-whole hierarchies. Thus, for example, the digestive system has several organs, each organ has critical parts, and each of those

parts has a complex morphology down to the level of individual cells and their parts and properties.

In the information domain, visual structure in microscopy is rarely described in visual terms. One rarely hears uniquely visual descriptors, such as "speckled", and one is unlikely to hear a phrase such as "bits of tubular structure." Rather, visual structure is described in terms of the target domain entities sampled by the slide and implied by the view of it. The bits of tubular structure might lead to a phrase such as, "this appears to be a glandular duct." Such a bias toward target domain semantics is similar to the human response to language. Language use aims at building a representation of semantics and quickly moves beyond an explicit consideration of phonology and syntax.

Questions about the Use of Visual Information

Although a study of discourse during the natural use of microscopes can reveal a great deal about visuocognitive skill, a full understanding of the mapping between visual information and the semantics of the target domain requires experimental studies that move beyond the display of whole microscope slides. Visual information must be systematically varied and the effects on recognition of microanatomy assessed.

There are numerous ways to analyze and vary visual structure in order to assess the information value of its components. As a first step in the study of microscopy, we analyzed visual information in microscope slides in terms of the structures that histologists refer to when they describe the slides: the various anatomical parts revealed in the tissue (e.g., Pani et al., 2005). Thus, when showing slide information for the pancreas, the pancreatic acini, islets of Langerhans, and exocrine ducts were each shown alone, in pairs, and with all three together. By comparing what is known from each of these presentations, a variety of basic questions about the mapping between target and information domains can be answered.

In an experiment to be described briefly here, several research questions were addressed for the various anatomical structures that compose each basic tissue in the histology curriculum. Perhaps the most basic questions pertained to the semantics of the visual structure when it is presented in terms of individual structures or small combinations of them. In particular:

--If students cannot provide a specific identification of a tissue, do they nonetheless correctly identify a higher taxonomic category (e.g., “gland”) or more inclusive anatomical system (e.g., “digestive system”)?

--If students misidentify a tissue, will it be for a tissue within the same higher-level category or anatomical system?

If these forms of partial recognition take place, it suggests that there is a dense mapping between components of visual structure and components of microanatomical knowledge, as well as an opportunistic use of visual structure to optimize access to the semantics of microanatomy.

A second set of questions concerned the manner in which visual information accumulates to provide complete access to the target domain. There are several basic options for how information might accumulate, and it seemed of fundamental interest to investigate this question here. Thus:

--Are single structures ever fully diagnostic of the tissue from which they were sampled? If so, is this common?

--As types of structure sampled from a tissue are increased in number, does visual diagnosticity increase also?

--Does visual diagnosticity appear only with (or increase suddenly with) particular combinations of structures?

--Is there a consistent pattern of information use across tissues, or does it vary from tissue to tissue?

--If students correctly identify tissues, do they also identify structures, consistent with the idea that recognition of component structures is used to infer the identity of the whole tissue?

Finally, there were several questions that arose from taking a cognitive science perspective in a domain of pre-existing professional expertise:

--How well does the use of information in recognizing microscope slides fit with the histologist’s concept of diagnosticity?

--Do students use subtle morphological differences for identification that histologists view dismiss as nondiagnostic?

Visual Recognition of Histological Structures

To address these questions, an experiment was conducted in which samples of tissue from microscope slides were shown to college students who had nearly completed the undergraduate course in histology. All possible combinations of single structures, pairs of structures, and higher level groups of structures from each basic tissue were shown. For example, the set of slides shown for pancreas is illustrated in Figure 2. Centroacinar cells were included in this case because this is a very small and hard-to-find structure that students are taught to recognize. A global low power slide also was included to see how a global overview compares with a more detailed view of the anatomical parts. The students were asked to identify the tissue as specifically as they could, but not to guess. After identifying the tissue, they were to identify any anatomical parts that they could.

Participants

Forty-two undergraduate students from the undergraduate college course in histology participated in a single session that lasted one and one-half hours. Nearly all of the students were biology majors, and most of them were in the premedical or pre-dental curriculum. All of the students (that were in the sample of 42 described here) received a grade of

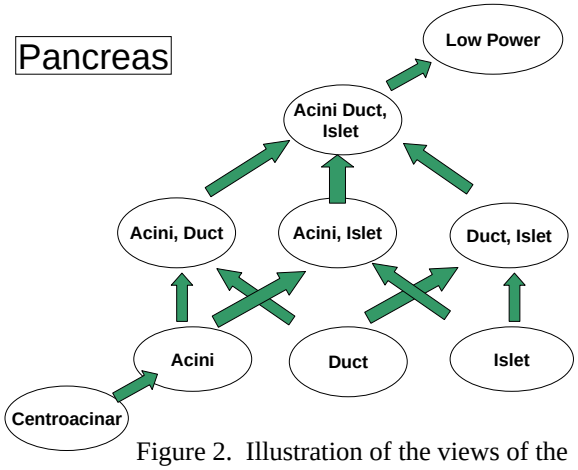

Figure 2. Illustration of the views of the pancreas shown in the experiment.

A, B, or C in the course. The experiment was conducted at the end of the semester, shortly before final examinations.

Method

Materials. Digital images of micrsocope slides were captured with a high resolution digital camera and stitched together with image processing software. Hundreds of images of histological structures and their combinations were prepared, and then prototypical/canonical views of them were selected for use in the experiment by the instructor of the histology course.

The images were standardized such that when projected to an overhead screen, global views of the tissue simulated a 4X magnification, and views of single structures and combinations of structures simulated a 20X magnification. The

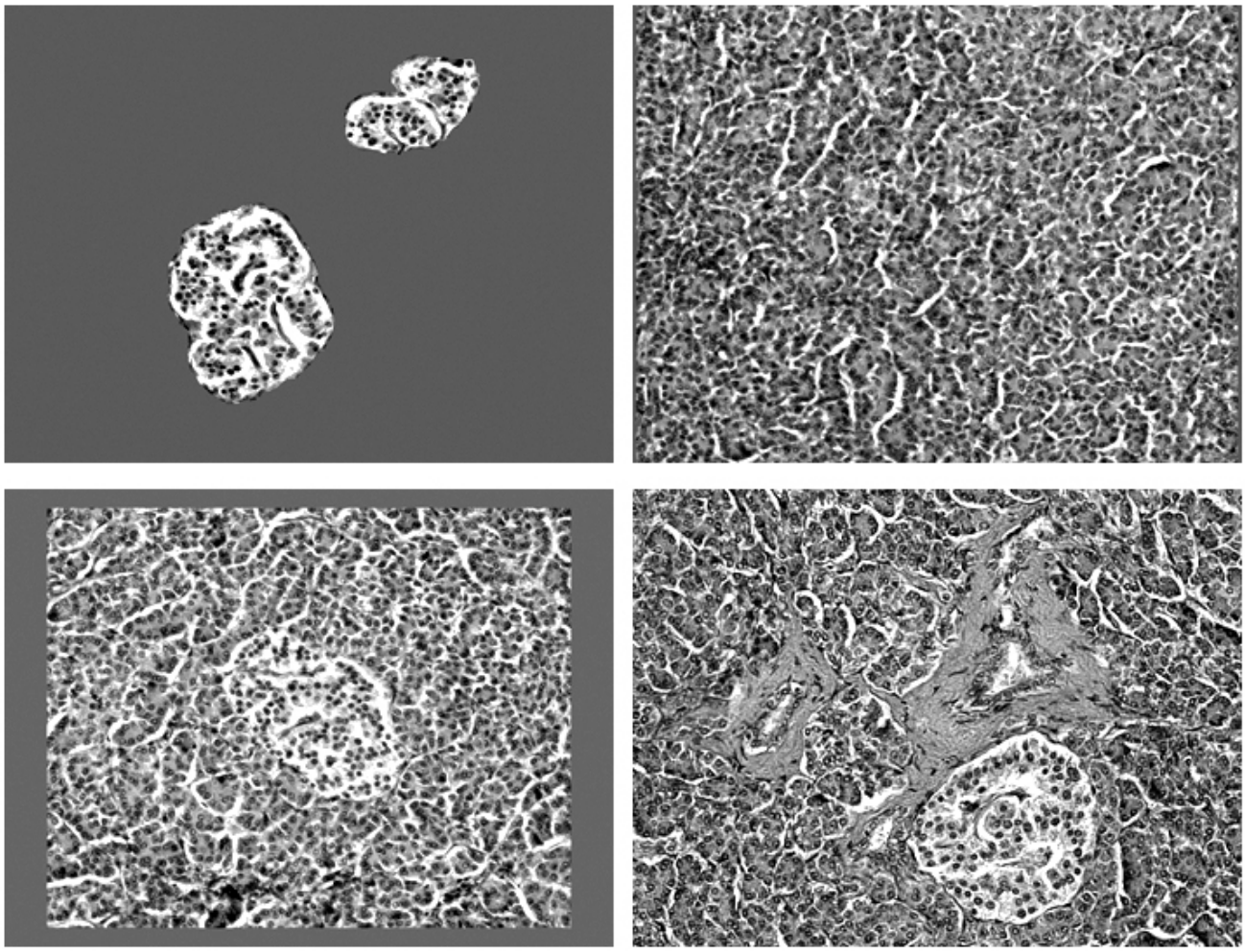

Figure 3. Examples of images presented to students in the experiment. All images show tissue from the pancreas. Beginning in the upper left, the images show the islets of Langerhans, the pancreatic acini, the islet and the acini together, and the islet, acini, and interlobular ducts together.

images were adjusted for brightness, contrast, and color so as to be the best possible natural views of the tissues.

Images were prepared for nearly all basic tissues that were covered in the histology course at the level of gland or organ. These were 18 different tissues/organs, including adrenal gland, colon, duodenum, esophagus, ileum, kidney, liver, lung, pancreas, parotid gland, pituitary gland, spleen, stomach, sublingual gland, thymus, thyroid, tonsil, and trachea.

The images showed the basic individual structures that compose each tissue and all possible combinations of those structures. When a structure naturally occurred next to, or was embedded within, another structure that it was combined with in the image, the image preserved that relationship. When combinations of structures not normally next to each other were displayed together, they were placed in separate boxes and shown side by side. The selective display of structures often required using image editing software to cover adjoining structures with gray, as illustrated in Figure 3.

Invariant details of the context of a structure were left in the slides when they were not part of a structure that would be selectively displayed in an alternative image. For example, if a duct is normally surrounded by connective tissue, the connective tissue was left in the image. Similarly, the glomerulus of the kidney typically is surrounded by a structure called Bowman's capsule, and this was shown in all images of glomeruli. No image of a structure or combination of structures was repeated.

Procedure. The images were projected to a large screen at the front of a standard classroom. They were presented with a projector mounted on the ceiling and controlled by a computer using Microsoft Powerpoint presentation software. Each slide was displayed for 40 seconds. To minimize bias from previous presentations, single structures were shown first, in random order, then combinations of two structures, and so on.

The students were asked to identify the tissue/organ from which the tissue shown in the slide was sampled, and then to identify the specific structure(s) that was shown in the slide. They were told to be as specific as possible, but to give a general answer if that was the best they could do. Multiple hypotheses were permitted, but they were not to guess.

Each student was given a packet to write down their answers. Each slide had its own section with separate lines for tissue and structure identification as well as a small black and white thumbnail of the image. Testing was done during the student's lab portion of the histology course. The experiment lasted for a total of one and half hours.

Results and Discussion

In regard to the basic questions about the semantics of visual structure when it is presented in terms of individual structures, or small combinations of them, it was clear that there is a dense and opportunistic mapping from visual structure to the semantics of the target domain:

-- If students don't recognize specific tissues do they identify tissues at a higher taxonomic category or in a larger anatomical system?

This is very common and is characteristic of the students' responses to the images. In the duodenum, for example, a slide showing muscle layers and intestinal villi led to identification of duodenum 0% of the time. However, participants knew the slide was from the small intestine 74% of the time. A slide of intestinal glands, villi, and Brunners glands led to identification of duodenum at a much higher rate: 60% of the participants could identify duodenum from the slide. An additional 33% of the participants knew that it was from the small intestine (93% total). Across 11 slides tested for identification of duodenum, identification was near 100% if higher level categories of small intestine, intestinal tract, and digestive system were counted as correct identifications.

The higher level identifications of tissue were sometimes at higher levels in a categorical taxonomy (e.g., submaxillary gland, salivary gland, gland). Much more often, however, the higher level terms were from a part-whole hierarchy (duodenum, small intestine, intestinal tract, digestive system). Once again, part-whole hierarchies organized around the system level (e.g., respiratory system) appear to be the primary form of organization for histological knowledge.

-- When students misidentify tissues, do they name tissues within the same anatomical category or system?

Just as students commonly resort to higher level descriptions, misidentification of a tissue for a different one that is within the same relatively narrow category or system is very common. For example, while 38% of the students could identify a sublingual gland from an image of glandular acini and the associated exocrine ducts, an additional 48% of the students misidentified it as a different salivary gland.

On the other hand, it is also common to see misidentifications based on visual features that are not due to common anatomy or physiology. For example, glomerular capsules of the kidney and islets of Langerhans from the pancreas are similar primarily in their both being small and round. Islets of Langerhans quite often led to a misidentification of kidney (38% of the time, compared with 36% correct identification of pancreas). Histologists refer to this phenomenon as the problem of "lookalikes".

Regarding the manner in which visual information accumulates to provide complete access to the target domain, every major option was observed for at least some tissues:

-- Do students ever identify tissues from seeing single structures?

The students did this quite often, although it was a small proportion of correct identifications overall. Table 1 shows the frequency of identification for several structures that might have been thought to be individually diagnostic of their larger tissues. Some single structures, such as the islets of Langerhans, are not individually diagnostic, even though they are described in those terms in histology texts.

Alveoli (from Lung)……	98%
Pars Distalis (from Pituitary)……..	52%
Islets of Langerhans (from Pancreas)..	36%
Brunner's glands (from Duodenum)...	17%

Table 1. Percentage identification of selected tissues from a single structure.

-- As structures are increased in number, does visual diagnosticity increase also?

This is quite a common pattern. Consider a measure of diagnosticity that was constructed for these data. If a slide was identified at the level targeted by the curriculum, the response was given a score value of 1.0. All other responses were recoded to the most specific structure or category in the body that would make the response correct. For example, if a participant misidentified a parotid gland as a salivary gland, the most specific category that would make the response correct would be gland. Thus, the least accurate responses could only be scored as "in the body". These responses were given a value of 5.0. Intermediate levels of specificity were assigned score values interpolated evenly between 1.0 and 5.0. Figure 4 shows the mean scores for the various images of the liver. Clearly some individual structures are more diagnostic than others, but it is equally clear that diagnosticity increases as more structures are added.

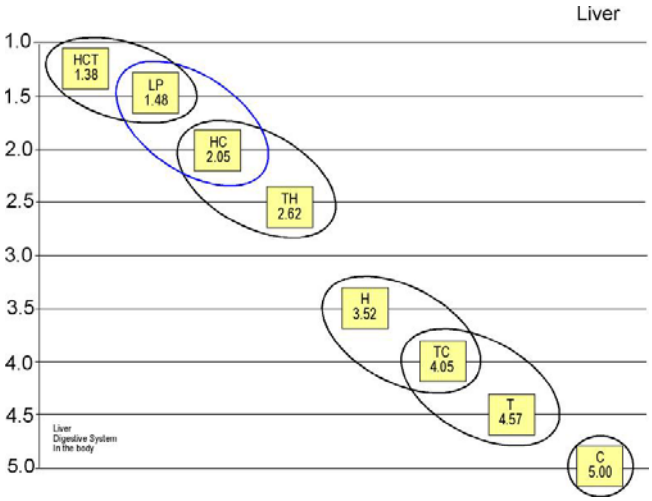

Figure 4. Variation in diagnosticity for different views of the liver. C is central vein, T is hepatic triad, and H is hepatocytes. Circles show images that were not statistically different from each other (Fischer's LSD).

-- Are certain combinations of structures substantially more diagnostic than would be predicted by the diagnosticity of the individual structures alone.?

This was evident in several instances, although again it was not ubiquitous. As one example, stratified squamous epithelium from the esophagus led to identification of esophagus 7% of the time. The muscularis mucosa led to identification 2% of the time. The epithelium together with the mucosa led to identification of esophagus 57% of the time.

-- Is there a general pattern of information use across tissues, or does it vary from tissue to tissue?

The specific manner in which visual information is used varies from tissue to tissue. While kidney and lung are easily identified from single structures, pancreas and liver depend on combinations of structures that are increasingly diagnostic as more are added. The morphological variation that allows unique identification does not replicate across tissues.

-- If students correctly identified tissues, do they also identify structures in them?

This is typical but not necessary. Thus, for example, of the 98% of the students who could identify lung from a view of the pulmonary acini, 85% of them went on to list the acini as the structure. On the other hand, 52% of the students identified the pituitary gland from a view of the pars distalis, but only 31% of those students went on to name the distalis. Thus, there is evidence consistent with the idea that tissue identification often is inferred from recognition of anatomical parts, but this does not appear to be necessary.

For the questions that arose from taking a cognitive science perspective in a domain of pre-existing professional expertise:

-- How well does psychological diagnosticity in perception map to the histological use of the term "diagnostic"?

Overall, not well. Islets of Langerhans, for example, must be seen in the context of surrounding acini to be highly diagnostic. And ducts in the kidney are highly diagnostic visually, although they are not generally described as being diagnostic by histologists.

The histologists' use of the term "diagnostic" refers to the objective nature of the anatomy. Islets of Langerhans are specific to the pancreas, and ducts are not specific to the kidney. It is now clear that the objective uniqueness predicts rather poorly the perceptual diagnosticity. Although ducts are not specific to the kidney, the students will tell you that, "Nothing else looks like that."

It is important to consider that in educational settings, the perceptual diagnositicity introduced by the cognitive scientist is equally as important as the objective description of the tissue that is favored in biology.

-- Do students use subtle morphological differences for identification that histologists consider nondiagnostic?

In general the answer is no. Table 2 shows percentage identification of tissues from seeing ducts characteristic of those tissues. The interlobular ducts from the pancreas, for example, led to identification of pancreas 0% of the time.

Table 2. Frequency of identifying tissue from seeing images of their ducts.

Pancreas	0%
Parotid	2%
Sublingual	0%
Kidney	90%

On the other hand, and as noted earlier, ducts from the kidney led to identification of kidney 90% of the time. Use of morphological variation among essentially similar structures appears to require very salient and consistent morphological characteristics. As shown in Figure 5, ducts in the kidney form a very salient pattern. This pattern occurs in nearly any slide from the kidney.

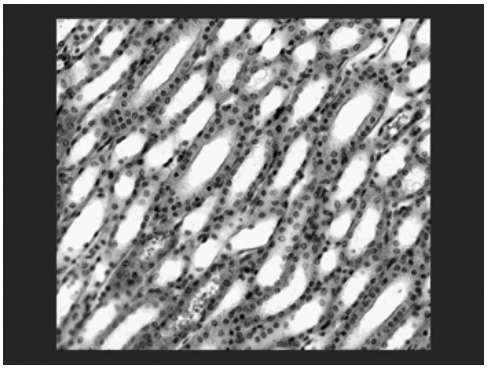

Figure 5. Collecting ducts from the kidney. Such compacted ducts are characteristic of the kidney and are nearly always recognized.

Conclusion

Graduates of a college course in histology have a well articulated model of anatomy that is composed of an extensive part-whole hierarchy in conjunction with certain categorical taxonomies. This knowledge is applied readily to visual perception of samples of tissue, such that nearly any structure that can be shown takes the student to an appropriate place in this well articulated knowledge system.

Students who have learned histology have found unique visual structures in microscope slides that map to their knowledge of anatomy at every level. A variety of patterns in the use of visual information develop as part of the effort to find the unique structures that provide full recognition of specific tissues. In some cases, single structures are diagnostic. In other cases, the larger the set of structures that are seen, the more specific is the recognition that follows. Finally, there are cases where only particular combinations of structures are effective for specific recognition.

The nature of this use of visual information is not predicted well by the biological description of the domain. Curriculum design will be well informed by the cognitive assessment of visual diagnosticity.

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