AUTHOR NOTE: the figure
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the fruit fly intestine, the hindgut, starts out as a simple tube along the embryo's midline. Through a process that occurs without cell division, this tube first dips ventrally (toward the fly's "belly"), and then rotates leftward by 90° to create a net rightward bend. Seeking a cellular basis for the rotation, Taniguchi *et al*. make the key observation of a small statistical bias in hindgut cell shapes with respect to the embryo's left-right axis. Cell-cell boundaries that make angles between −90° and 0° with the tube's long axis (left boundaries) appear more frequently than boundaries that make angles between 0° and 90° (right boundaries). The authors call this pattern planar cell-shape chirality (PCC). They identify the cell-cell adhesion molecule *Drosophila* E-cadherin (*D*E-cadherin) as a factor required for both PCC and gut rotation, showing that it is preferentially enriched on left boundaries. Mutations in a motor protein involved in intracellular movement, known as unconventional myosin ID (*MyoID*), reverse the polarity of *D*E-cadherin accumulation and PCC. This is consistent with *MyoID*'s previously identified role in setting the direction of gut rotation (*5*, *6*).

Because mutations in *D*E-cadherin cause all cell boundaries to expand, Taniguchi *et al*. suggest that *D*E-cadherin limits boundary expansion by increasing boundary tension. They propose that left-biased tension is sufficient to produce a leftward tissue rotation. Indeed, computer simulations identify one possible mechanism by which this might work. First, left-biased tension drives cell shape change and rearrangement while the endpoints of the tube remain fixed. Then, rotation occurs in the absence of asymmetric tension, and the tube twists as the cells relax back toward more regular shapes.

Together, Tang *et al*. and Taniguchi *et al*. highlight how statistical differences in cell behavior across a large population can lead to stereotyped, tissue-level morphogenesis. They also highlight several key ways in which mathematical models provide an essential predictive bridge between cell- and tissue-level dynamics. In the mouse lung, it is intuitively clear that biases in cell division orientations could cause differential increases in tube length versus circumference, and previous work had shown that oriented cell divisions can contribute to tube shape (*7*–*10*). A model, however, was essential to show quantitative sufficiency. In the case of the fruit fly hindgut, it is far from obvious how biasing tension on left boundaries will produce a leftward twist. Here, mathematical models step in when intuition fails, and provide plausible testable hypotheses.

For both systems, the mathematical models provide a framework for exploring the molecular mechanisms that control local cell polarity and coordinate its tissue-wide effects. One obvious candidate in both cases is the signaling pathway known as the planar cell polarity (PCP) pathway, which controls cell division orientations and cellular polarities in many other contexts (*11*, *12*). In the experiments conducted by Tang *et al*. and Taniguchi *et al*., however, disrupting PCP function had no effect on these developmental processes, suggesting that other mechanisms are at work.

In the mouse lung, a key question is: How does ERK signaling shape the distribution of cell division angles? The nature of the wild-type distribution suggests that cells partition between two qualitatively distinct orientation states: strictly longitudinal or random. Tang *et al*. hypothesize that the longitudinal state is the default, that ERK signaling overrides this default to randomize division axes, and that *Spry1/2* tune ERK signaling to achieve a balance between longitudinal and random divisions. But how does a graded change in ERK levels control the fraction of cells that inhabit these two states? Does ERK signaling merely gate the response to a longitudinal cue, or does it directly control a transition between distinct phenotypic states?

Likewise, the Taniguchi *et al*. study provides a starting point for thinking about how local left-right asymmetries in force generation could drive chiral rotation, but how do these asymmetries arise? The observation that *MyoID* mutants exhibit reversed PCC and gut rotation implies an intrinsic mechanism for breaking chiral symmetry that can be biased in either direction. The genetic requirements for *D*E-cadherin and MyoID suggest that symmetry breaking occurs shortly before hindgut rotation and requires local interaction across cell-cell boundaries. By contrast, in vertebrates, establishment of left-right asymmetry occurs far in space and time from the organs undergoing chiral morphogenesis, which suggests that it may be easier to identify the mechanisms involved.

These studies signal a growing trend in which classical molecular and genetic approaches merge with quantitative microscopy, image analysis, and modeling to provide new insights into the cellular dynamics of tissue morphogenesis. It is likely, however, that we are seeing just the tip of an iceberg.

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PSYCHOLOGY

Sentence and Word Complexity

Jeffrey Heinz[1] and William Idsardi[2]

Do humans learn the sentence and sound patterns of natural languages through distinct learning mechanisms?

Our understanding of human learning is increasingly informed by findings from multiple fields—psychology, neuroscience, computer science, linguistics, and education. A convergence of insights is forging a "new science of learning" within cognitive science, which promises to play a key role in developing intelligent machines (*1*, *2*). A long-standing fundamental issue in theories of human learning is whether there are specialized learning mechanisms for certain tasks or spheres of activity (domains). For example, is learning how to open a door (turning the handle before pulling) the same kind of "learning" as putting up and taking down scaffolding (where disassembly must be done in the reverse order of assembly)? Surprisingly, this issue plays out within the domain of human language.

Language perception is organized at different levels, each with its own internal organizing principles: the organization of sounds into words (phonology), the organization of roots and affixes into words (morphology), and the organization of words into phrases into sentences (syntax). Are there any differences among the patterns observed at each level? And if there are, are specialized or

[1]Department of Linguistics and Cognitive Science, University of Delaware, 42 East Delaware Avenue, Newark, DE 19716, USA. [2]Department of Linguistics and Program in Neuroscience and Cognitive Science, University of Maryland, 1401 Marie Mount Hall, College Park, MD 20742, USA. E-mail: heinz@udel.edu

nonspecialized learning mechanisms better or worse at explaining them?

Theoretical computer science provides a mathematically rigorous way to characterize patterns in terms of strings, i.e., sequences of more basic units. For example, sentences are sequences of words; words are sequences of sounds. Patterns in any domain can be described as a set of strings or a probability distribution over strings. The Subregular and Chomsky hierarchies (3) arrange all logically possible patterns into nested regions of complexity (see the figure). These regions have multiple, convergent definitions which distill the necessary properties of devices (such as grammar, in the case of language) that can recognize or generate the strings comprising the pattern (or, in the case of distributions, their probabilities). This mathematical framework permits the comparison of patterns and their complexity across different levels or domains, linguistic or otherwise.

Every natural language distinguishes well-formed and ill-formed sentences and words. Every sentence in this article is well-formed; ill-formed sentences are obtained by shifting every period one word to the left. Likewise, English words must contain proper sequences of English sounds (4). For example, "gdansk" and "srem" are not possible native English words, though they are possible words in other languages. English speakers can readily assent to new coinages ("bling") while avoiding others ("gding").

An important, but perhaps overlooked, difference is that sound patterns are less complex than sentence patterns according to the Subregular and Chomsky hierarchies. Capturing which patterns of words are well-formed sentences can require context-free or even mildly context-sensitive computations (5). Thus, similar to the assembly and disassembly of scaffolding, English exhibits recursion, because sentences ("The mouse ran away") can be contained in larger ones ("The mouse that the cat chased ran away"). The recursive nature of sentence patterns is a defining characteristic of natural language (6), and demonstrably makes such sentence patterns at least context-free.

By contrast, sound patterns are measurably simpler because identifying well-formed patterns of sounds does not require context-free computations (7). One kind of sound pattern restricts adjacent sounds (such
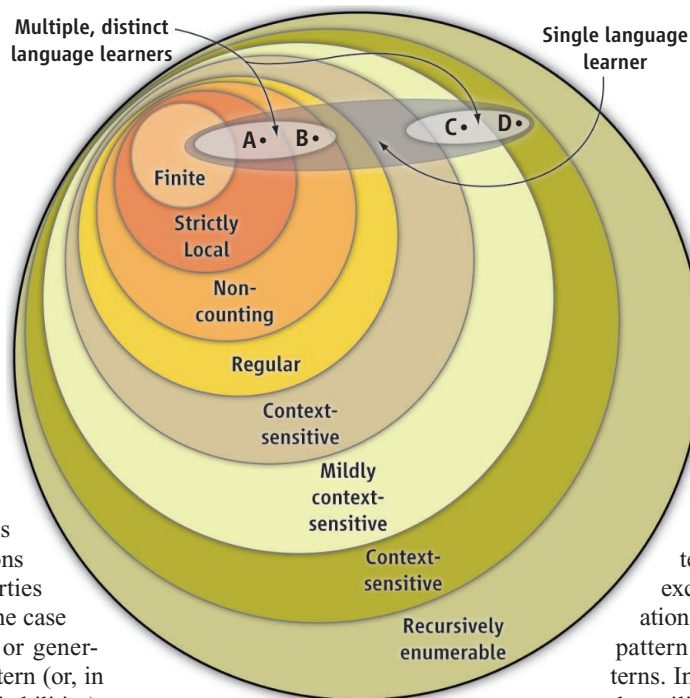
Complexity hierarchies for patterns. The Subregular and Chomsky hierarchies divide all logically possible patterns into nested regions (4). A is a pattern of permissible consonant clusters in English (14); B is the long-distance sound pattern of Samala (9); C is the recursive pattern of sentences within sentences in English; D is a particular sentence pattern in Swiss German (5).

as "gding"). Another kind of sound pattern restricts sounds over long distances (8). For example, Samala, a language native to California, does not allow words containing both "s" and "sh." Consequently, there are words such as "shtoyonowonowash" (which means "it stood upright") but none like "shtoyonowonowas" (9). Moreover, all sound patterns fall into the "regular" region (less restricted) of the Chomsky hierarchy (7), and probably belong to even less complex regions (10).

What are the possible explanations for this computationally measurable difference between sentence patterns and sound patterns? One possibility is that sound patterns are constrained by the human nervous, motor, and auditory systems in ways that sentence patterns are not. That is, the moment-to-moment configurations of the vocal tract constrain the moment-to-moment articulation of sounds. However, long-distance sound patterns cannot be due to articulation alone because the tongue does not retain the "sh" posture throughout "shtoyonowonowash."

Because humans do learn languages, another possibility is that the properties of sentence patterns and sound patterns reflect properties of how they do this. It follows that if humans employ distinct learning mecha-

nisms for phonology and syntax, the complexity differential could be explained. There is a convergence of results from philosophy, psychology, and computer science (1, 11–13), showing that learning is only possible if learners (humans or machines) are restricted in the generalizations they are allowed to consider. Indeed, the successes in the "new science of learning" carefully tailor hypothesis spaces so that learners succeed with reasonable amounts of data and effort.

In fact, recent, distinct computational models for learning sound patterns (10, 14) and sentence patterns (15, 16) succeed because they exclude certain patterns from consideration. For instance, algorithms for sound-pattern learning exclude context-free patterns. In this way, these results demonstrate the utility of multiple, differentiated algorithms for language learning.

Task-specific knowledge and its acquisition are familiar in robotics (17) and biology (18). Human and robot locomotion, for example, are often modeled with systems with less than context-free power (19). Thus, modular learning proposals may be based not on the content of the domains (language versus locomotion), but rather on the informational complexity of the patterns in each domain.

Although single, general-purpose language-learning models (20) cannot be ruled out, they face a series of challenges. Such models predict that no complexity differential between sound patterns and sentence patterns should exist: Any sentence pattern ought to be a possible sound pattern and vice versa. Moreover, such unitary algorithms must enable the learning of both sound patterns and sentence patterns from reasonable amounts of data. Finally, these models should also offer some explanation for the observed difference in complexity between sentence and sound patterns (or disprove it).

While complexity differentials do not entail distinct learning mechanisms, the hypothesis that humans learn sound patterns separately from sentence patterns provides a viable explanation for the difference in complexity observed between them. The utility of specialized or general learning mechanisms (or perhaps even both) for language learning will become clearer through further empirical collaborations. Indeed, psychologists and linguists are currently testing these hypotheses with artificial language-learning experiments (21), an approach that can determine

whether people make the same kind of generalizations when they encounter both words and sentences.

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CHEMISTRY

Pores Within Pores—How to Craft Ordered Hierarchical Zeolites

Thin walls of crystalline zeolites can be assembled into hexagonal nanopore networks, which expands the range of their catalytic reactions to larger molecules.

Karin Möller and Thomas Bein

Zeolites are aluminosilicate crystals that have internal networks of angstrom-size pores, similar to the dimensions of small molecules. They are among the most widely used materials in heterogeneous catalysis (*1*, *2*) because of their defined structure and composition. Although zeolites are very potent solid-acid catalysts, their catalytic applications have been limited to processing smaller molecules; their internal pores are not readily accessed by molecules exceeding 1 nm in size. Major efforts have been directed to overcoming this limitation. On page 328 of this issue, Na *et al.* (*3*) present a new strategy for creating thin zeolite walls, containing small pores, that grow into structures forming larger pores that can catalyze reactions with larger molecules.

To date, two major synthesis strategies have been explored to create zeolites with additional larger pores. One is to form a secondary pore system of larger size than the zeolitic micropores within the zeolite crystal, thereby allowing faster diffusion of larger molecules into the zeolite particles. In many zeolite synthesis routes, molecular "templates" are added to aid the growth of the aluminosilicate crystals; when the synthesis is completed and the template molecules are removed, zeolitic pore spaces remain. Traditional methods in zeolite synthesis use a single molecular template with a size similar to or smaller than the micropore dimensions. This micropore size barrier was broken in the early 1990s with the synthesis of mesoporous oxides by using larger amphiphilic surfactant templates (*4*). However, the local order in the resulting (alumino-)silicates was lost, and with it their strong acidity. Efforts to recrystallize these amorphous walls into zeolitic structures were usually unsuccessful.

Dual-templating approaches are now being explored that combine the advantages of zeolites and the mesoporous oxides. In addition to the molecular zeolite templates, larger assemblies such as the above surfactant micelles (*5*), polymers (*6*), or objects such as carbon beads or fibers (*7*) were used to create mesoporosity. Alternative approaches include chemical treatments that partially dissolve the crystalline zeolite lattice and create larger intraparticle cavities (*8*). The need for a secondary template can also be avoided by the direct assembly of nanosized zeolite particles, thus creating mesoporous interparticle voids (*9*).

The other approach for allowing access of larger molecules to zeolite pores is to pre-
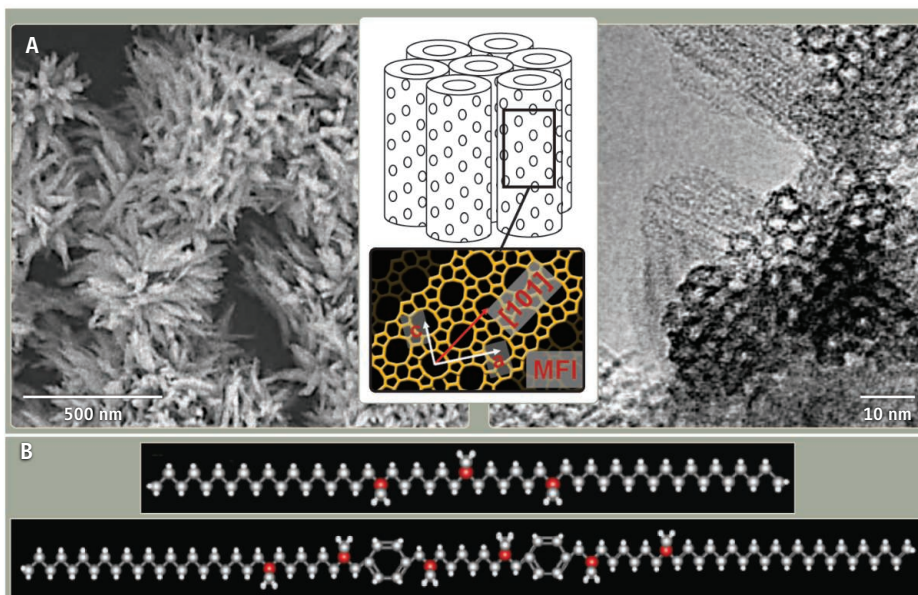
Ordering the walls. Na *et al.* have used large molecular templates to grow thin walls of zeolites into morphologies that create ordered mesopores. (**A**) Two electron microscopy images of the hexagonally grown mesoporous MFI-type zeolite with extremely high surface area. The inset shows a schematic of the hierarchical structure and the MFI pore framework of the zeolite walls. (**B**) Examples of the bifunctional templating molecules used in the synthesis that bear ammonium groups and long alkyl chains (white spheres, hydrogen; gray spheres, carbon; red spheres, nitrogen).

Department of Chemistry, Ludwig-Maximilians University, 81377 Munich, Germany. E-mail: karin.moeller@cup.uni-muenchen.de; bein@lmu.de

Multiple, distinct language learners

Single language learner
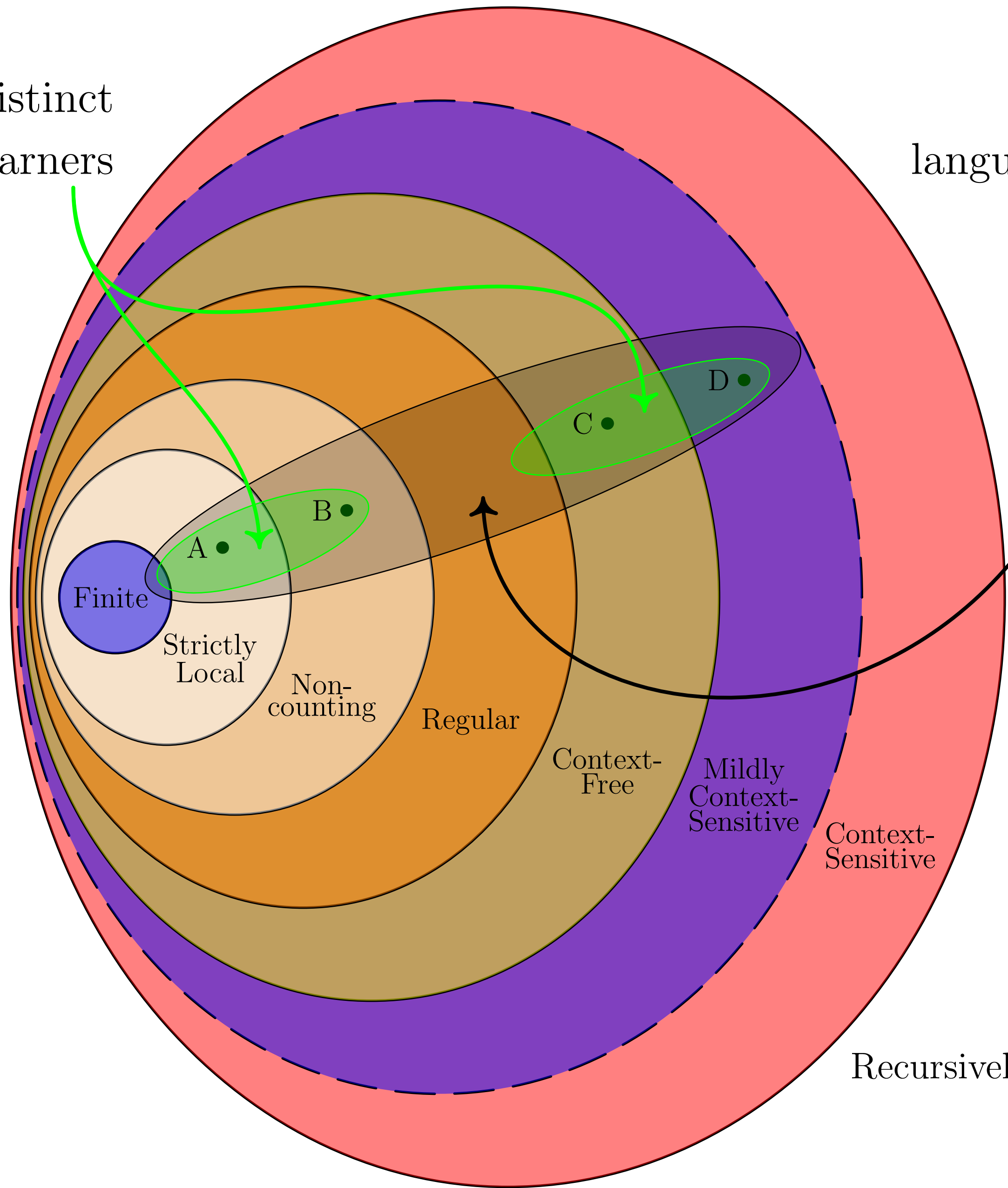
Finite

Strictly Local

Non-counting

Regular

Context-Free

Mildly Context-Sensitive

Context-Sensitive

Recursively Enumerable

A

B

C

D