angstroms in size ensures that they move much more rapidly than the atomic nuclei. For metallic (conduction) electrons in solids that are delocalized over large distances, electron translational energies can be much smaller and the separation of time scales need not necessarily hold.

In recent years there has been a flurry of new work casting doubt on the validity of the Born-Oppenheimer approximation for reactions at metals. These include the failure of the standard model to accurately account for the experimentally observed N_2 vibrational excitation in the recombination of N atoms desorbing from ruthenium (*6*) and in another case the incidence energy dependence of O_2 dissociative adsorption on aluminum (*7, 8*). In our laboratory, we performed experiments showing that hundreds of kilojoules of vibrational energy per mole can be transferred from a "hot molecule" to electrons of a metal; this work culminated in the observation of vibrational promotion of electron emission from a metal with a low work function (*9*, *10*). This result showed explicitly, by direct detection of the hot electron essentially blown off the surface by the force of the molecular vibration, that the Born-Oppenheimer approximation broke down. The topic of Born-Oppenheimer breakdown has become an active forefront area of research in surface chemistry.

Nieto *et al.* show that despite these clear indications of the importance of Born-Oppenheimer breakdown, one is not precluded from using the standard model of reactivity in all cases. In other words, there certainly are some reactions at metal surfaces (perhaps most; time will tell) that are well described by the standard model of reactivity. In this work, comparisons are made between experiment and theory in one of the simplest and best characterized surface chemical reactions, H_2 interacting with a platinum surface. It is noteworthy that Nieto *et al.* are able to use a highly sophisticated version of the standard model, where six degrees of freedom are treated quantum mechanically—a technical tour de force. The 6D quantum approach is essential because H_2 and H exhibit quantum interference (wave behavior) effects as a result of their low masses. When H_2 collides with platinum, it may bounce off and diffract quantum mechanically or dissociate, forming adsorbed H atoms on the surface. The first-principles simulation of H_2 on platinum reported by Nieto *et al*. captures in a nearly quantitative fashion both of these very different kinds of collisional processes. This is a remarkable success for the standard model of reactivity and provides new motivation to seek the limits of this approach, which have not yet been identified clearly.

Future work will certainly focus on helping to better define under what conditions the standard model of reactivity can be applied to catalytically important reactions at metal surfaces. In addition, theorists are actively striving to develop the next generation of chemical simulation packages that can take into account the role of excited electronic states in surface chemistry, going beyond the Born-Oppenheimer approximation. Such developments will make important contributions to our understanding of all kinds of chemistry involving excited electrons in solids. For example, our ability to learn how to power catalytic processes with light (photocatalysis) as opposed to heat (conventional thermal catalysis) will rely on new understanding of excited states in solids, an area of future technology that is essential to a world with diminishing cheap oil reserves.

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DEVELOPMENTAL BIOLOGY

Mixed Messages in Early Development

MicroRNAs, molecules that repress gene expression, fine-tune early embryogenesis. Rather than expressing genetic information supplied in the egg from the mother, microRNAs direct the developing embryo to express its own genome instead.

Stephen M. Cohen and Julius Brennecke

During oogenesis, the egg is loaded with nutrients, proteins, and messenger RNAs (mRNAs) produced in the ovary by the mother. Many of these "maternal mRNAs" encode proteins that are needed for early development of the embryo, before the onset of new mRNA synthesis that is directed by the embryo's own genome. Soon after fertilization of the egg, a transition occurs from use of maternal mRNAs to expression of the zygotic genome (see the figure). On page 75 of this issue, Giraldez and co-workers report that the zebrafish microRNA-430 (miR-430) family contributes to this transition by promoting turnover of maternal mRNAs (*1*).

MicroRNAs (miRNAs) are small noncoding RNAs that serve as posttranscriptional regulators of gene expression (*2*, *3*). They provide sequence information needed to guide ribonucleoprotein complexes (miRNPs) to target mRNAs, leading to repression of their translation and enhanced turnover. The 5′ end of a miRNA, called the seed region, confers much of the target recognition specificity. Computational and experimental studies have shown that miRNAs typically have hundreds of target sites in a given transcriptome, most often located in the 3′ untranslated region (3′ UTR) of a target mRNA (*4*–*7*). Recent studies based on miRNA target prediction and on comparison of miRNA and target mRNA expression suggest that miRNAs may help to reduce expression of mRNAs to inconsequential levels in cells where they are no longer needed or where their expression might be detrimental (*8*, *9*).

The new findings by Giraldez *et al*. provide an elegant example of this principle in action. In previous work (*10*), they identified miR-430 as an abundant early expressed miRNA in the developing zebrafish embryo. Subsequent cloning efforts showed that miR-430 is the only abundant miRNA in the first 4 to 8 hours of development (*11*). miR-430 is encoded by a large gene family (more than 90 members) that produces several, slightly different, forms of the mature miRNA. Because these miRNAs are expressed at the same time and place and share the same seed sequence, they are expected to have largely overlapping sets of targets. Expression of miR-430 begins at the moment of transition from maternal to zygotic gene expression, and mature miR-430 rapidly accumulates to high levels.

In view of the complexity of the miR-430 gene family, generating mutant zebrafish that lack it would be a daunting task. However, because this miRNA is the only one expressed

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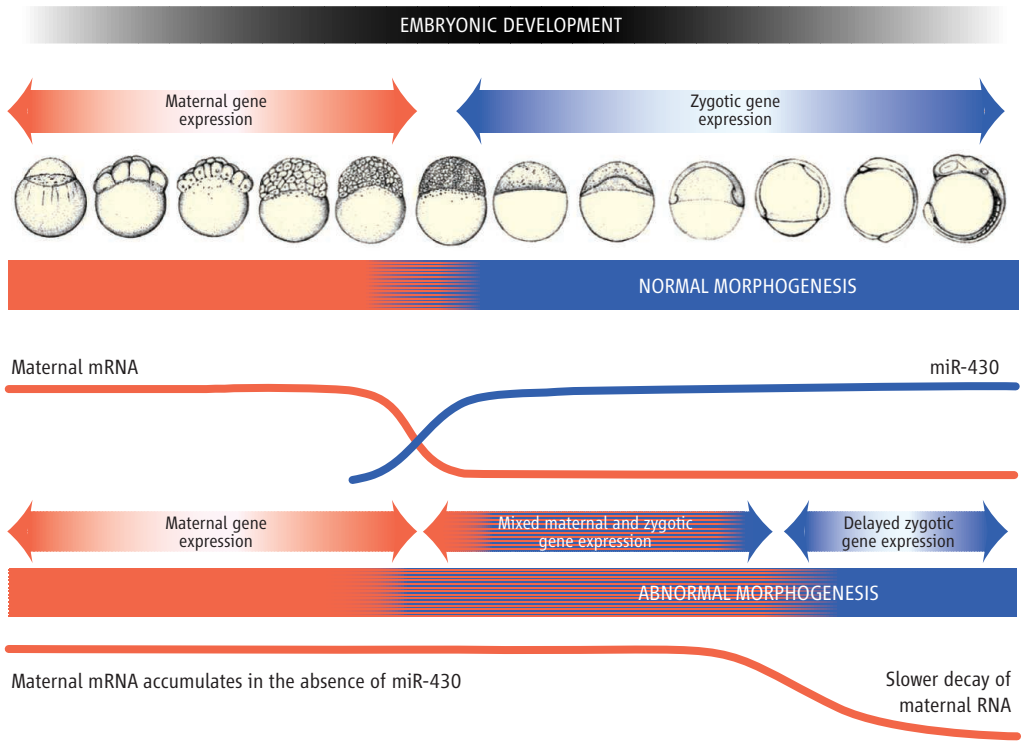
so early in the embryo, the authors were able to apply a clever trick to produce embryos lacking it. The ribonuclease III enzyme Dicer processes miRNA precursors to produce mature miRNAs. Dicer is provided to the egg as a maternal mRNA in amounts sufficient to support embryonic development, but it is also expressed zygotically (*12*). With the use of germ cell transplantation, it is possible to produce adult female fish that have a germline lacking Dicer activity. These fish can then be used to produce "Dicer-free" embryos that are incapable of processing miRNA precursors and, as such, lack mature miRNAs. Dicer-free embryos exhibit subtle defects in gastrulation and brain morphogenesis, most of which can be suppressed by injecting the embryo with mature miR-430 (*10*).

Giraldez *et al*. used this method to assess the effects of miR-430 on mRNA levels in the early zebrafish embryo. By comparing expression profiles of Dicer-free embryos to those of embryos supplemented with miR-430, they estimate that several hundred mRNAs are likely to be direct targets of destruction by miR-430 in the early embryo. Remarkably, about 40% of maternal mRNAs may be affected. This genome-wide analysis is substantiated by extensive experiments showing that regulation of many of the identified targets is posttranscriptional and mediated by their 3′ UTRs, and that a subset of these depend on the presence of the identified miRNA target sites. Thus, the biological effects can be attributed to a direct interaction between miR-430 and the targets.

How does miR-430 control the abundance of these RNAs? A miRNA can induce cleavage of a target mRNA if the degree of sequence complementarity between them is high enough. That, however, is rarely the case in animals. Nonetheless, miRNAs can reduce the level of many mRNAs that contain only imperfect target sites (*13*). Recent work suggests that miRNAs direct their targets to P-bodies, cytoplasmic foci where rapid mRNA decapping and degradation occur (*14*–*16*). Yet the mechanistic link between miRNP binding and target mRNA localization to P-bodies has remained unclear. Giraldez *et al*. add to this picture by showing that miR-430 promotes the rapid deadenylation of target mRNAs. The polyadenosine tail of a mRNA contributes to its stability and enhances mRNA translation into protein. Polyadenylation of maternally deposited mRNAs is an important regulator of their expression in the embryo. Giraldez *et al*. found that target mRNAs were adenylated on schedule but were then rapidly deadenylated, limiting the window for efficient expression. This rapid deadenylation required the presence of miR-430 and its target sites in the 3′UTR of the regulated mRNAs. Another recent report (*17*) suggests that target mRNA deadenylation is a general consequence of miRNP recruitment. Whether deadenylation is the primary cause of target accumulation in P-bodies or vice versa remains to be determined.

Perhaps the most intriguing outcome of this study is the finding that miR-430 targets maternal mRNAs to promote their turnover. A consequence of removing miR-430 activity is that these mRNAs are not cleared efficiently and continue to be present, and presumably translated into protein, for longer than normal. This situation at least partially blurs the transition from maternal to zygotic control of embryonic development (see the figure). In view of the resulting substantial shift in gene expression, it seems surprising that mixing maternal and zygotic mRNAs does not have more profound consequences for the embryo. Presumably, these maternal mRNAs eventually decay, but they do so more slowly than in the presence of miR-430. This study provides compelling support for the emerging view that many miRNAs fine-tune development to ensure robustness, rather than act as developmental switches (*8*, *9*). Early and abundant expression of miR-430–related miRNAs is conserved among vertebrates, so the function of these miRNAs in the maternal-zygotic transition may be a general feature of vertebrate embryogenesis, even though very different maternal mRNAs may have acquired target sites over time in different species.



Fine-tuning embryonic development. In early zebrafish embryogenesis, the microRNA miR-430 regulates the transition from maternal to zygotic mRNA transcription by targeting maternal mRNAs for degradation. In the absence of miR-430, maternal mRNAs accumulate and interfere with morphogenesis. [Adapted from (*10*)]

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