high enantioselectivity and good yield were observed for aryl methyl ketones, with a modest drop in enantioselectivity for electron-poor substrates. Other aryl ketones gave rise to good to excellent e.r.'s, as highlighted by substrate **2h**. Heteroaromatics were also well tolerated under the reaction conditions, with thiophene- and furan-derived ketones undergoing highly enantioselective propargylation reactions (**2i** and **2j**). Additionally, an α,β-unsaturated ketone was an excellent substrate for enantioselective propargylation, leading to a 95:5 e.r. (**2p**).

In the case of aliphatic ketones, the catalyst selected on the basis of steric differentiation, giving higher e.r.'s with increased steric bulk on a single side of the ketone (**2l** to **2o**). An e.r. of 85:15 observed for 2-hexanone (**2l**) is relatively impressive, considering that the catalyst is differentiating a methyl from an *n*-butyl group. Groups with substitution at the α-position of the ketone substantially enhanced the e.r.'s, as highlighted by ketones with a cyclohexyl (96:4 e.r., **2n**) and a *t*-butyl group (98:2 e.r., **2o**). Furthermore, a γ-butyrolactone (**2q**) could be synthesized with a good e.r. from propargylation of an aliphatic ketone with a pendant ester.

Our data suggest that steric-electronic correlations provide a means for efficient optimization of a catalytic system and are evidence for a synergistic relationship between these two classically independent variables in reactions. This is especially attractive for optimizing reactions with limited detailed mechanistic and structural understanding and, considering that the modeling is tied to basic physical organic precepts, a greater understanding of the underlying features of asymmetric catalysis should result. The application of this method is not limited to asymmetric catalysis but can potentially be applied to broad areas of chemistry dependent on evaluating the interplay of two (or more) effects on a reaction outcome.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/333/6051/1875/DC1
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References (*48*, *49*)

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Diurnal and Seasonal Mood Vary with Work, Sleep, and Daylength Across Diverse Cultures

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We identified individual-level diurnal and seasonal mood rhythms in cultures across the globe, using data from millions of public Twitter messages. We found that individuals awaken in a good mood that deteriorates as the day progresses—which is consistent with the effects of sleep and circadian rhythm—and that seasonal change in baseline positive affect varies with change in daylength. People are happier on weekends, but the morning peak in positive affect is delayed by 2 hours, which suggests that people awaken later on weekends.

Individual mood is an affective state that is important for physical and emotional well-being, working memory, creativity, decision-making (*1*), and immune response (*2*). Mood is influenced by levels of dopamine, serotonin, and other neurochemicals (*1*), as well as by levels of hormones (e.g., cortisol) (*3*). Mood is also externally modified by social activity, such as daily routines of work, commuting, and eating (*4*, *5*). Because of this complexity, accurate measurement of affective rhythms at the individual level has proven elusive.

Experimental psychologists have repeatedly demonstrated that positive and negative affect are independent dimensions. Positive affect (PA) includes enthusiasm, delight, activeness, and alertness, whereas negative affect (NA) includes distress, fear, anger, guilt, and disgust (*6*). Thus, low PA indicates the absence of positive feelings, not the presence of negative feelings.

Laboratory studies have shown that diurnal mood swings reflect endogenous circadian rhythms interacting with the duration of prior wakefulness or sleep. The circadian component corresponds to change in core body temperature, which is lowest at the end of the night and peaks during late afternoon. The sleep-dependent component is elevated at waking and declines throughout the day (*7*). Other studies have variously observed a single PA peak 8 to 10 hours after waking (*8*), a

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plateau from noon to 9 p.m. (*6*), and two daily peaks at noon and evening (*4*) or afternoon and evening (*5*). Some PA studies have also reported a "siesta effect" or midafternoon dip (*6*). Results for NA have also been inconclusive, with peaks observed in the midmorning (*4*) as well as the afternoon (*4*, *5*) and evening (*5*). Several studies have also found that NA is not subject to diurnal variation (*6*, *8*).

Although these studies have improved our understanding of affective rhythms, they have relied heavily on small homogeneous samples of American undergraduates (*5*, *6*, *8*) who are not necessarily representative of the larger population (*9*). Students are exposed to varying academic schedules that constrain when and how much they sleep. Further, these studies typically rely on retrospective self-reports, a method that limits temporal granularity and is vulnerable to memory error and experimenter demand effects. Researchers have acknowledged the limitations of this methodology (*10*) but have had no practical means for in situ real-time hourly observation of individual behavior in large and culturally diverse populations over many weeks.

That is now changing. Data from increasingly popular online social media allow social scientists to study individual behavior in real time in a way that is both fine-grained and massively global in scale (*11*), making it possible to obtain precise real-time measurements across large and diverse populations.

Several recent studies have examined the affective and semantic content of messages from online sources such as Twitter, a microblogging site that records brief, time-stamped public comments from hundreds of millions of people worldwide (*12*–*15*). Using data from Twitter, O'Connor *et al*. (*13*) found that opinions about specific issues and political candidates varied from day to day. Dodds and Danforth (*14*) showed how the affective valence of songs, musicians, and blog posts depends on the day of week, especially holidays. In an unpublished study, Mislove *et al*. (*16*) used Twitter messages to examine what they refer to as the "pulse of the nation" as it varies across the week and moves across time zones. While avoiding the data limitations of an earlier generation of laboratory-based experiments, these studies, by computer and information scientists, conflate diurnal changes within each individual with baseline differences in affect across individuals of different chronotypes (sleep-wake cycles), who tend to be active at different times of the day. If "morning people" and "night owls" differ in baseline affect, this will confound within-individual changes in affect from morning to night. These studies also collapsed positive and negative affect into a single dimension, contrary to previous research that has consistently shown these to be largely independent dimensions. As a consequence, the reported patterns cannot be unambiguously interpreted.

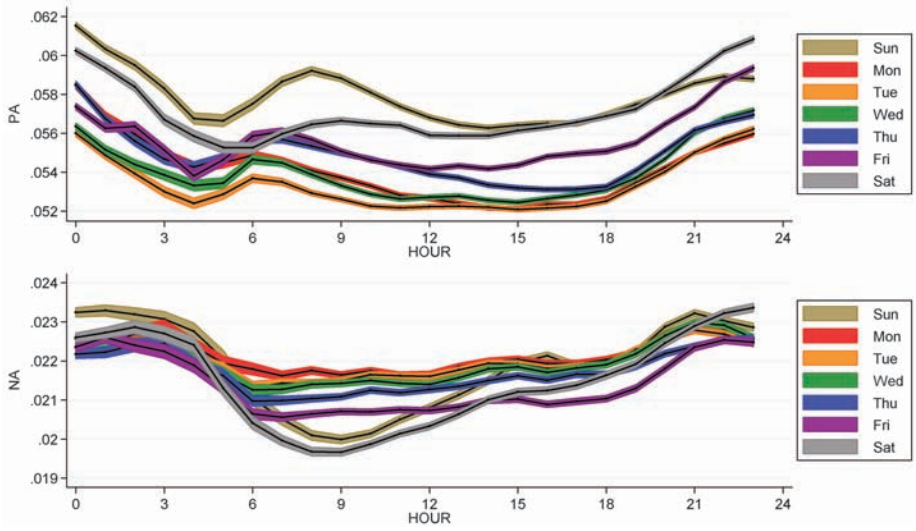

Fig. 1. Hourly changes in individual affect broken down by day of the week (top, PA; bottom, NA). Each series shows mean affect (black lines) and 95% confidence interval (colored regions).

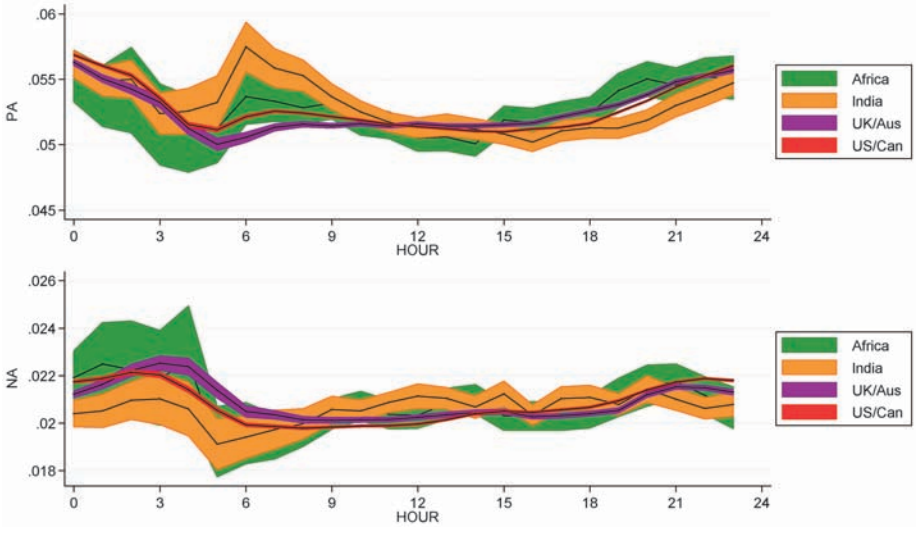

Fig. 2. Hourly changes in individual affect in four English-speaking regions. Each series shows mean affect (black lines) and 95% confidence interval (colored regions).

Our study also uses data from Twitter, whose 140-character limit on message length allows conversation-like exchanges. Text analysis of these messages provides a detailed measure of individuals' spontaneous affective expressions across the globe. We measured PA and NA using Linguistic Inquiry and Word Count (LIWC), a prominent lexicon for text analysis (*17*). The LIWC lexicon was designed to analyze diverse genres of text, such as "e-mails, speeches, poems, or transcribed daily speech." LIWC contains lists of words or word stems that measure 64 behavioral and psychological dimensions, including PA and NA, as well as "anxiousness," "anger," and "inhibition." These lists were created using emotion rating scales and thesauruses and validated by independent judges. Bantum and Owen (*18*) found that for all emotional expression words, LIWC's sensitivity and specificity values were 0.88 and 0.97, respectively. We used a lexicon containing only English words, and all reported results include only English speakers; the English proficiency measure is described in (*19*) and its distribution is shown in fig. S5.

We analyzed changes in hourly, daily, and seasonal affect at the individual level in 84 identified countries (table S2). In contrast to the self-report methodology used in offline studies, these measures were not prompted by an experimenter, or recollected after the fact. Rather, they were directly obtained from comments composed by the individuals in real time, and are therefore less vulnerable to memory bias and experimenter demand effects. Most important, instead of relying on a small sample of American undergraduates, we measured affective changes among millions of Twitter users worldwide, allowing cross-societal tests of cultural and geographic influences on affective patterns.

Using Twitter.com's data access protocol, we collected up to 400 public messages from each user in the sample, excluding users with fewer

than 25 messages. The resulting corpus contained about 2.4 million individuals from across the globe and 509 million messages authored between February 2008 and January 2010 (tables S1 to S4).

We removed between-individual differences by mean-centering the measures of PA and NA at the individual level (*19*). (Between-individual effects are shown in fig. S2). Figure 1 shows hourly and daily changes in within-individual PA and NA for English-speaking individuals worldwide, in local time, including 95% confidence intervals. The shapes of the affective rhythms were nearly identical across days of the week for both PA and NA. PA had two peaks: relatively early in the morning and again near midnight. Although the shape of the rhythm was consistent across days, PA levels were generally higher on Saturday and Sunday ($M = 0.058$) than at any time during the weekdays ($M = 0.054$, $P < 0.001$), which points to possible effects of work-related stress, less sleep, and earlier wake time. PA decreased midmorning (at the start of the work day) and increased in the evening (at the end of the work day). However, the fact that the shape of the affective cycle was similar on weekends and weekdays points to sleep and the biological clock as important determinants of affect, regardless of variations in environmental stress. Moreover, the morning (3 a.m. to noon) peak on Saturday and Sunday was delayed by nearly 2 hours ($M = 9{:}48$ a.m. versus $M = 7{:}55$ a.m., $P < 0.001$)—the amount of time that people might be expected to "sleep in," allowing themselves to be awakened, not by the alarm clock, but by the body clock.

NA was lowest in the morning and rose throughout the day to a nighttime peak; this pattern also suggests that people may be emotionally "refreshed" by sleep. Relative to PA, NA varied less with the exception that the morning trough was lower on the weekend. The pattern also supports the assumption that PA and NA vary independently and are not opposite ends of a single dimension. NA is neither the mirror image of PA, nor do the two measures move consistently in parallel. This independence is reflected in the small correlation ($r = -0.08$).

These patterns varied for individuals of different chronotypes. Most people are most active in the afternoon and evening (*19*), and message volume is highest between 9 a.m. and 10 p.m. (fig. S1). However, "night owls," or people most active late at night, exhibited markedly different rhythms in both PA and NA (fig. S3).

Despite these differences between chronotypes, the temporal affective pattern is similarly shaped across disparate cultures and geographic locations. Figure 2 shows diurnal rhythms (based on local time) for four groups of countries: United States and Canada; United Kingdom, Australia, Ireland, and New Zealand; India; and English-speaking Africa. Although the rhythms across these regions are not statistically indistinguishable [$\chi^2(69, N = 226{,}777{,}910) = 852{,}557$, $P < 0.001$], the patterns mirror those observed in Fig. 1: a morning rise and nighttime peak in PA, and a sharp drop in NA during the overnight hours.

This similarity is consistent with a biological explanation based on the correspondence between the circadian clock and sleep (*20*), but sleep patterns in turn partially depend on the organization of the work day and work week. For most of the developed world, people typically work Monday to Friday from 9 a.m. to 5 p.m. However, in the United Arab Emirates, the traditional work week runs Sunday to Thursday (*21*). This allowed for a natural experiment: If diurnal rhythms are affected by sleep schedules that are shaped by cultural norms, we would expect Friday and Saturday in the UAE to have higher baseline PA and a later morning peak than during the rest of the week. This was confirmed by the daily and weekly pattern in the UAE, which mirror the global patterns, with higher PA on the weekend (Friday and Saturday; $M = 0.057$) than during the work week (Sunday to Thursday; $M = 0.055$, $P < 0.001$) and a delayed PA peak on Friday and Saturday of nearly 2 hours ($M = 9{:}53$ a.m. versus 8:04 a.m., $P < 0.001$). Although the work day in the UAE begins earlier than it does in the west (*21*), the UAE does not differ in the timing of its morning PA peak.

The importance of sleep and the biological clock for affective rhythms may extend beyond diurnal rhythms to seasonal patterns as well. However, like diurnal mood studies, previous research on seasonal mood changes has relied on small samples within single countries and is severely constrained by the difficulty of collecting data over an entire year (*22*). Clinical research has found higher prevalence of depressive anxiety during winter at more northern latitudes (*23*). Although this was originally attributed to insufficient exposure to light (*23*), more recent research on seasonal mood variation supports the "phase-shift hypothesis," which points to the importance of the timing of the dawn signal to synchronize the circadian pacemaker (*24*).

We therefore examined how PA and NA vary within individuals with seasonal changes in daylength. The length of the day at a given location varies sinusoidally over the year, with higher-amplitude waves the farther one moves from the equator, resulting in long summer days and short winter days in extreme latitudes and consistent daylength equatorially. Daylength is modeled using two parameters, latitude and day of the year (*25*). We then used the slope of the line tangent to the daylength curve, which indicates whether the summer solstice (positive slope) or winter solstice (negative slope) is approaching (*19*), to measure relative change in daylength. We also measured absolute daylength as the interval between sunrise and sunset. Figure S4 illustrates these measures.

We found no effect of absolute daylength on either PA ($r = 3.14 \times 10^{-5}$, $P = 0.905$) or NA ($r = -5.14 \times 10^{-4}$, $P = 0.052$). However, as predicted by the phase-shift hypothesis, we observed a change in affect with relative daylength. Figure 3 shows the best-fitting line through 14.3 million observations (affect by minutes gained or lost per day), as well as the 95% confidence interval. (For visual reference, we also superimposed 100 aggregate observations binned by percentiles.) The positive slope in the upper panel of Fig. 3 shows baseline PA (averaged over each person-month) is higher when change in daylength is positive (as the summer solstice approaches) than when it is negative (as the winter solstice approaches) ($r = 1.21 \times 10^{-3}$, $P < 0.001$) and is highest when change in daylength is greatest, at the spring equinox. In contrast, NA does not change ($r = 1.86 \times 10^{-4}$, $P = 0.483$). This result supports survey-based findings that show seasonal changes in PA but not NA (*26*), and suggests that "winter blues" (*27*) is associated with diminished PA but not increased NA.

Although the analysis of online messages makes it possible to track changes in affect in

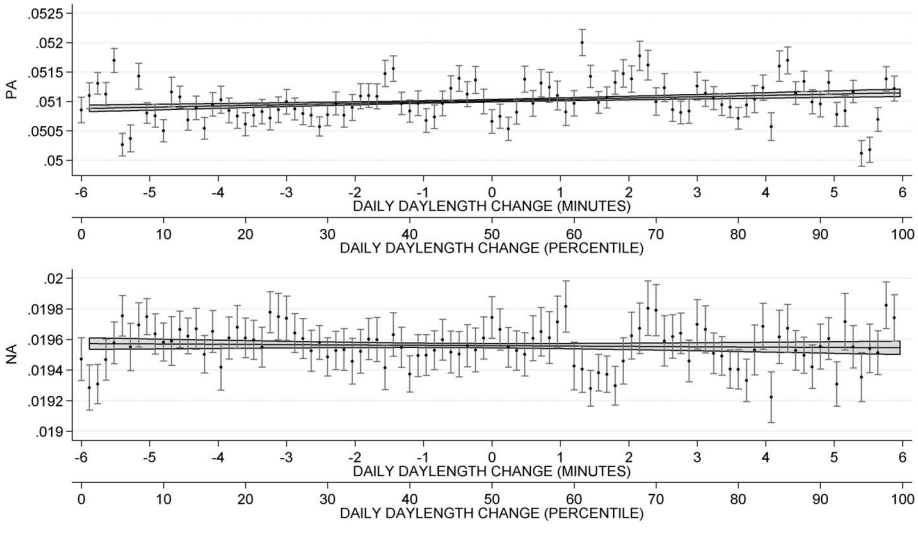

Fig. 3. Line of best fit through the 14.3 million person-month observations (affect by minutes gained or lost per day). For visual reference, 100 aggregate observations binned by percentiles are superimposed.

ways that are not feasible offline, there are also important limitations. First, unlike laboratory studies, we have little data on conditions that are known to influence mood, including demographic and occupational backgrounds that may influence when and how much people sleep, the level and timing of environmental stress, susceptibility to affective contagion, and access to social support. Second, lexical analysis measures the expression of affect, not the experience. Cultural norms may regulate the appropriateness of affective expression at different times of the day or week. Because these norms are unlikely to be universal, the robust patterns we observed across diverse cultures (as well as across days of the week) give us confidence that affective expression is a reliable indicator of diurnal individual-level variations in affective state.

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Supporting Online Material

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Histone Lysine Demethylase JARID1a Activates CLOCK-BMAL1 and Influences the Circadian Clock

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In animals, circadian oscillators are based on a transcription-translation circuit that revolves around the transcription factors CLOCK and BMAL1. We found that the JumonjiC (JmjC) and ARID domain–containing histone lysine demethylase 1a (JARID1a) formed a complex with CLOCK-BMAL1, which was recruited to the *Per2* promoter. JARID1a increased histone acetylation by inhibiting histone deacetylase 1 function and enhanced transcription by CLOCK-BMAL1 in a demethylase-independent manner. Depletion of JARID1a in mammalian cells reduced *Per* promoter histone acetylation, dampened expression of canonical circadian genes, and shortened the period of circadian rhythms. *Drosophila* lines with reduced expression of the *Jarid1a* homolog, *lid*, had lowered *Per* expression and similarly altered circadian rhythms. JARID1a thus has a nonredundant role in circadian oscillator function.

To gain insight into the dynamics of chromatin modifications and the function of CLOCK-BMAL1 transcription factors in the circadian clock, we measured the state of two histone modifications that correlate with active transcription, acetylation of histone 3 (H3) lysine 9 (H3K9Ac), and trimethylation of H3 lysine 4 (H3K4me3) at the *Per2* promoter (*1*). In mouse liver, both modifications synchronously oscillated at the *Per2* gene promoter CLOCK-BMAL1 E2–binding site ("E-box") (*2*), with lowest amounts at circadian time (CT, the endogenous, free-running time) 3 hours after the onset of activity (CT3) and peak amounts at CT12 (Fig. 1A). The peaks of histone modification were followed by those of *Per2* mRNA abundance. We also found BMAL1 abundance rhythms at the E-box, which reached a maximum at CT9 (Fig. 1B). Histone acetyltransferases (HATs) and histone deacetylases (HDACs) generate rhythms in histone acetylation and have important roles in circadian rhythms (*3*, *4*). H3K4me3 modification at promoter regions correlates with transcriptional potential, which suggests that this mark helps maintain a transcriptionally poised state (*5*). Recently, the H3K4 methyltransferase MLL1 was shown to have a necessary role in CLOCK-BMAL1–dependent transcription (*6*).

We focused on a JumonjiC (JmjC) domain–containing H3K4me3 demethylase family with four mammalian and one insect gene members (fig. S1). In murine liver chromatin, JARID1a was enriched at the *Per2* E-box, and its profile at this site coincided with that of BMAL1 (Fig. 1B). *Jarid1a* expression in liver did not show robust oscillations (fig. S2), which suggested that recruitment of JARID1a to the *Per2* promoter might be mediated by the circadian machinery. Indeed, JARID1a recruitment to the *Per2* promoter E-box but not at a non–CLOCK-BMAL1 JARID1a target is reduced in *Bmal1*$^{-/-}$ cells (Fig. 1C and fig. S17A). Consistently, immunoprecipitation of endogenous CLOCK or BMAL1 from nuclear extracts copurified with endogenous JARID1a (Fig. 1D). Similarly, CLOCK and BMAL1 associated with immunoprecipitated JARID1a (fig. S3). Overexpression of JARID1a enhanced CLOCK-BMAL1–mediated transcription from *Per2* (Fig. 1E) and *Per1* (fig. S4A) promoters in a dose-dependent manner but failed to coactivate expression from an unrelated (E74-Luc) reporter (fig. S4D). Furthermore, coactivation of CLOCK-BMAL1 by JARID1a did not require its histone demethylase activity, as JARID1a mutants that carry a loss-of-function mutation (H483A, in which Ala replaces His^{483}) (*7*) or that lack the JmjC domain enhanced CLOCK-BMAL1 activity, reversed

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