Vibrational Sonification and Visual Sigil of Zwitterionic Glycine as a Prototype Audio-Visual Stimulus for Human Sleep Thermoregulation

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Article

Vibrational Sonification and Visual Sigil of Zwitterionic Glycine as a Prototype Audio-Visual Stimulus for Human Sleep Thermoregulation

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Abstract

Glycine has been proposed as a temperature linked neuromodulator of human sleep, acting through nitric oxide mediated vasodilation and peripheral heat loss. Several small randomized trials suggest that pre-sleep oral glycine can modestly improve subjective sleep quality and next-day performance, but the mechanistic bridge between molecular structure, thermoregulation, and sleep remains largely untested. This study develops and documents a non-chemical representation of glycine that can be used as a prototype stimulus for future experiments. We first assembled a zwitterionic vibrational model of glycine from infrared and Raman data, and linearly mapped each normal mode from wavenumber to audio frequency so that 1600 cm^{-1} corresponds to 300 Hz, preserving the relative spectral pattern. On this fixed molecular spectrum we constructed two complementary 5 minute audio stimuli. The primary research stimulus applies a compressed oral like pharmacokinetic envelope to all modes, using a one compartment absorption elimination curve with parameters derived from published human glycine half life estimates and explicitly treated as order of magnitude constraints rather than precise population kinetics. In parallel, we generated an artistic evaporation reference in which higher frequency modes fade earlier than lower skeletal modes, organized into four qualitative stages that were designed by chemical intuition rather than fitted to data. Finally, we encoded the same vibrational groups in a concentric visual sigil and a short animation that can be paired with the audio. Together, these open source tools provide a transparent, molecule linked prototype for testing whether structure derived audio patterns influence thermoregulation, sleep related physiology, or subjective experience in future ethically reviewed studies. No new human or animal data are collected in this work; all clinical information is drawn from published trials, and the audio-visual materials are presented as a design prototype for future ethically reviewed studies.

Keywords: glycine; sleep; thermoregulation; nitric oxide; pharmacokinetics; molecular sonification; audio stimulus; visual sigil

1. Introduction

Glycine and L-serine are closely interconnected amino acids with long histories in biochemistry, nutrition, and neuroscience. Both participate in one-carbon metabolism and neurotransmission, and both have been implicated in the control of body temperature and sleep timing [1,2]. Recent work links pre-sleep oral glycine to modest improvements in subjective sleep quality and next-day performance in adults with chronic sleep complaints, while basic science studies show that glycinergic and serinergic signalling can interface with nitric-oxide-mediated thermoregulation in the suprachiasmatic nucleus (SCN) and in peripheral vasculature [1–4]. Within this context, the present study does not introduce a new chemical intervention, but instead develops a non-chemical, molecule-linked audio-visual prototype that encodes the structure of zwitterionic glycine for future, ethically reviewed experiments.

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1.1. Glycine and Serine in Thermoregulation and Sleep

Glycine operates through at least two complementary mechanisms that are relevant to sleep. First, as an inhibitory neurotransmitter acting at glycine receptors and as a co-agonist at N-methyl-D-aspartate (NMDA) receptors, it modulates synaptic gain in circuits that link the SCN, brainstem, and spinal cord [2,3]. Second, in both animal and human experiments, pre-sleep glycine ingestion has been associated with peripheral vasodilation, mild reductions in core body temperature, and improved thermal comfort at sleep onset [1–4]. L-serine, while not the main subject of this work, contributes through two metabolic routes: conversion to glycine via serine hydroxymethyltransferase, which feeds glycinergic and NMDA co-agonist signalling, and its role as a precursor in phospholipid and sphingolipid synthesis that may influence membrane-level gating processes [2,3]. Together, glycine and serine sit at an intersection of inhibitory neurotransmission, metabolic support, and temperature-linked sleep initiation.

1.2. Nitric Oxide and the Thermoregulatory Sleep Gate

Nitric oxide (NO) has been repeatedly proposed as a mediator between circadian timing, vascular tone, and sleep onset [3–7]. Activation of glutamatergic and glycinergic inputs to the SCN can engage neuronal nitric oxide synthase, leading to NO production and downstream changes in vasoactive mediators and autonomic output [3,4]. In both experimental animals and human thermophysiology studies, a characteristic pattern emerges: distal skin temperature rises, proximal skin and core temperature show small compensatory changes, and this distal-proximal gradient predicts shorter sleep-onset latency [5–7]. Blocking NO synthesis, or experimentally preventing heat loss from the extremities, impairs this temperature-dependent sleep gate [3–7]. Within this picture, glycine is one of several modulators that can influence NO generation, vasodilation, and the ease with which the body crosses the thermoregulatory threshold into sleep.

1.3. Botanical and Cultural Origin of Glycine Intake

From a nutritional perspective, most glycine in human circulation comes from a combination of dietary protein, bone and connective-tissue rich foods, and endogenous synthesis from serine [8–11]. Serine itself is produced mainly through the phosphorylated serine pathway from the glycolytic intermediate 3-phosphoglycerate, via phosphoserine aminotransferase and phosphoserine phosphatase, with serine hydroxymethyltransferase transferring a one-carbon unit to tetrahydrofolate and feeding the folate-linked C1 pool [8–11]. In this metabolic network, serine and glycine are tightly coupled and interchangeable at the level of C1 traffic, yet glycine itself is the downstream molecule of interest in this paper because it is the form most consistently linked to NO-mediated thermoregulation, inhibitory transmission, and pre-sleep clinical trials [1–4,8–11].

In leaves of C3 crops, glycine levels are strongly shaped by photorespiration: two molecules of glycine are decarboxylated by the glycine decarboxylase complex and serine hydroxymethyltransferase, releasing CO2, ammonia, and reducing equivalents, and regenerating serine [8–11]. This glycine-to-serine conversion occurs at very high rates in the leaves of wheat, rice, soybean, and other staple crops whenever they are photosynthesizing. In animal feed and human diets, additional glycine-rich pools appear in collagen, gelatin, skin, tendons, and slow-cooked meat, shifting the balance between glycine, serine, and other amino acids in a way that may matter for long-term one-carbon metabolism and vascular health [8–14].

Globally Important Crops as Glycine Reservoirs

At the food-system level, a small group of crops supplies most dietary energy and protein for humans and their livestock: wheat, rice, maize, soybean, sugar crops, and oilseed families dominate both acreage and trade [15–22]. Many of these plants, especially C3 cereals and legumes, have strong photorespiratory fluxes and substantial glycine pools in photosynthetic tissues [8–11,15–22]. When these crops are processed into grain, flour, oil, or feed, a fraction of this glycine is preserved or

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reconstituted in by-products such as bran, germ, and press cakes; another fraction reappears later in animal-source foods produced from animals raised on these feeds [15–22]. Together, these plant groups form a global glycine web linking plant metabolism, feed formulation, and human diets.

Cultural Foodways and Perceived Calming or Warming Effects

Across diverse food cultures, similar plant and animal sources recur in dishes that are perceived as calming, sleep-supportive, or warming in the evening: slow-cooked broths and stews rich in gelatin and connective tissue; soy-based dishes; wheat-based porridges and breads; and combinations of grains and legumes in comfort foods [18–22]. These dishes combine glycine and serine with many other bioactive compounds, and their effects on mood or sleep cannot be attributed to glycine alone [18–22]. Nevertheless, they illustrate how specific glycine-linked ingredients and textures are embedded in long-standing cultural practices, which may have been informally tuned to thermal comfort and sleep over generations.

Bridging to Clinical and Mechanistic Approaches

Taken together, this botanical and cultural background supports a view of glycine as both a biochemical node and a food-system node: a small amino acid that participates in one-carbon metabolism, collagen turnover, neurotransmission, and NO-mediated vasodilation, while also being concentrated in specific plant families, connective tissues, and traditional dishes. Serine remains an important upstream partner, but the present study restricts its focus to glycine as the molecule that currently has the most direct clinical and mechanistic evidence for influencing pre-sleep thermoregulation and subjective sleep quality [1–4,8–14]. This provides a biologically grounded starting point for constructing non-chemical experimental probes based on the structure of glycine rather than on additional dosing.

1.4. Audio Patterning and Auditory Beat Stimulation in Physiology

A substantial literature demonstrates that structured auditory stimulation can modulate human physiology via autonomic and central mechanisms. Systematic reviews of music and auditory stimulation report consistent, if modest, effects on cardiac autonomic indices: preferred or relaxing music tends to increase high frequency heart rate variability (reflecting parasympathetic activity), reduce low frequency to high frequency ratios, and lower blood pressure compared with silence or non preferred sound, although heterogeneity and risk of bias remain important limitations [24].

Within this broader field, auditory beat stimulation, most notably binaural beats, provides a more parametric approach in which the frequency difference between two tones defines the beat. A systematic review by Ingendoh and colleagues concluded that binaural beats can, under some conditions, entrain brain oscillations in the targeted frequency band, but that results are highly dependent on parameters and many studies report null findings [25]. A meta-analysis by Garcia Argibay and colleagues similarly found small but significant effects of binaural beats on anxiety, pain perception, and some cognitive outcomes, with considerable heterogeneity across protocols [26]. More recent narrative and systematic reviews focused on clinical and psychiatric populations, such as the work by Askarpour and colleagues, echo this pattern: binaural beats show promise as an adjunct for anxiety and mood, yet overall effect sizes are modest and not uniformly replicable [27].

Several randomized controlled trials specifically document autonomic and hemodynamic effects of auditory beat stimulation. In a double blind, placebo controlled, within subject study, McConnell and colleagues exposed participants to 6 Hz theta frequency binaural beats during post exercise recovery and observed increased high frequency heart rate variability and reduced low frequency to high frequency ratios compared with placebo tones, indicating enhanced parasympathetic activation and sympathetic withdrawal [28].

Perioperative and procedural settings provide further evidence that auditory beat stimulation can influence both subjective anxiety and cardiovascular responses. In a randomized controlled trial

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of patients undergoing cataract surgery under local anesthesia, Wiwatwongwana and colleagues compared music with embedded binaural beats, music alone, and no music. The binaural beat group showed greater reductions in anxiety scores and lower systolic blood pressure and heart rate than controls [29]. Additional trials in cataract surgery and other elective procedures report that binaural beat music can reduce operative pain and anxiety and attenuate tachycardic responses relative to standard care or non beat audio [30,31].

At the same time, several controlled studies and systematic reviews emphasize that not all protocols are effective. Some experiments fail to detect changes in brain activity, mood, or autonomic indices beyond those produced by music or relaxation alone, and publication bias cannot be excluded [25,27]. Taken together, the current evidence supports a cautious conclusion: auditory beat stimulation can influence brain oscillations and autonomic balance in humans, but its effects are modest, context dependent, and sensitive to frequency band, carrier tones, exposure duration, listening posture, and individual differences.

In the context of the present work, this literature provides the physiological foundation for extending auditory interventions into a new class of stimuli: molecule derived sonifications. If relatively simple beat based modulations of pure tones can alter heart rate variability, blood pressure, and perioperative anxiety under controlled conditions, it is biologically plausible, though untested, that more complex but precisely defined patterns derived directly from glycine vibrational modes could also interact with neurovascular and thermoregulatory control. In this project we therefore construct two related stimuli from the same zwitterionic glycine peak list: a primary pharmacokinetic based stimulus whose envelope follows a compressed 0-4 hour absorption-elimination profile, and a secondary evaporation reference stimulus that stages group specific envelopes as a chemist's artistic representation of an evaporating molecular layer. Both retain a one-to-one mapping between audible partials and molecular modes. The glycine sonification framework thus builds on established principles of sound induced physiological modulation while introducing a mechanistic anchor at the level of molecular structure, which can now be explored empirically in future studies without implying any proven clinical effect. The sonification is anchored in glycine's molecular structure rather than in nitric oxide dynamics themselves; its connection to NO-mediated physiology is therefore indirect and remains an empirical question. Importantly, the present sonification does not implement auditory beat stimulation or target specific beat frequencies; ABS is cited here only as evidence that structured audio can interact with physiological state under controlled conditions.

1.5. Objective

The objective of this work is to define and technically characterise a family of glycine-linked stimuli that can be used as open, reusable prototypes in future experimental studies. Specifically, we construct two 5 minute audio stimuli whose spectra are fixed by the vibrational modes of zwitterionic glycine: a primary stimulus in which all modes are modulated by a compressed pharmacokinetic-style envelope derived from published human glycine half-life estimates, and a secondary evaporation reference in which higher-frequency modes fade earlier than lower skeletal modes according to a qualitative, chemistry-inspired design. In parallel, we build a visual sigil and short animation that encode the same vibrational groupings. The goal is not to claim therapeutic effects, but to provide well documented, molecule-derived tools that allow researchers to test whether such structure-based audio-visual patterns can measurably influence thermoregulation, sleep-related physiology, or subjective experience in ethically reviewed human or animal studies.

2. Methods

2.1. Clinical Data Handling: Pre-Sleep Glycine Trials

Methods and inclusion criteria

This section summarizes human clinical trials in which oral glycine was given in the pre-sleep period and at least one sleep-related outcome was reported. We considered randomized controlled

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trials and controlled crossover studies in adults, and excluded open label, uncontrolled, or purely observational reports. Trials were required to clearly state dose, timing, outcome measures, and basic participant characteristics. For each study we extracted: sample size, age range, inclusion criteria, glycine dose and timing, placebo or control condition, primary and secondary sleep endpoints, and main findings.

2.1.1. Subjective Sleep Quality in Adults with Chronic Sleep Complaints

Inagawa et al. investigated whether low dose glycine taken shortly before bedtime could improve subjective sleep quality in adults with chronic sleep complaints [1,2]. In a randomized, single blind, crossover design, participants received either glycine (3 g in water) or placebo 30 minutes before their usual bedtime for several nights, followed by a washout and condition switch. Subjective sleep quality and next-day fatigue were assessed using visual analogue scales and simple daytime performance tasks. Glycine modestly improved self rated sleep quality and reduced morning fatigue relative to placebo, without producing residual sedation or serious adverse events at this dose and duration.

2.1.2. Subjective and Objective Sleep in Adults with Sleep Complaints

Yamadera et al. extended this work by combining subjective and objective measures in adults with sleep complaints [3]. In a randomized, double blind, crossover trial, participants consumed 3 g glycine or placebo 30 minutes before bedtime for several nights, while polysomnography and core body temperature were recorded. Glycine was associated with small improvements in sleep onset latency and sleep efficiency, and with a tendency toward reduced nocturnal core temperature in the early night, consistent with a facilitated thermoregulatory sleep gate. Daytime sleepiness and performance were not adversely affected, and no clinically meaningful adverse events were reported.

2.1.3. Glycine Under Partial Sleep Restriction

A third line of work examined glycine under conditions of experimental sleep restriction [4]. In a within subject design, healthy adults underwent partial sleep deprivation and received either glycine or placebo prior to the truncated sleep opportunity. The primary outcomes were next-day performance on cognitive tasks and self-reported fatigue. Glycine did not fully normalize performance but attenuated some of the subjective and objective decrements compared with placebo. As in the other trials, the dose was 3 g given shortly before the reduced sleep episode, with no serious safety signals in the time frame studied.

2.1.4. Methodological quality and limitations

Taken together, these trials suggest that pre-sleep oral glycine at a dose of 3 g can modestly improve subjective sleep quality and next-day functioning under specific conditions and in relatively small samples [1–4]. However, their methodological limitations are substantial. Sample sizes are in the tens rather than hundreds of participants; most studies involve relatively healthy adults with chronic sleep complaints or experimentally induced sleep restriction, rather than patients with severe insomnia or significant medical comorbidities; and follow up is short, typically limited to days or a few weeks. Outcome measures vary across trials, with a mix of visual analogue scales, simple cognitive tasks, polysomnography, and core temperature recordings, making direct comparison difficult. We therefore did not attempt a formal meta-analysis, because the available trials are few in number, heterogeneous in design and outcomes, and often lack the detailed reporting needed for reliable pooled effect estimates. Throughout the manuscript, these pre-sleep oral glycine trials are used primarily as motivation and boundary conditions for designing the audio and visual prototype, and no inference is made that molecule derived audio will reproduce the magnitude or specificity of their ingestion effects.

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There is also little formal pharmacokinetic characterization of glycine in the context of these sleep trials. Published pharmacokinetic observations instead come mainly from peri operative settings in which glycine containing irrigation fluids are infused during surgery and plasma concentrations are followed during and after the procedure. These small series, usually in older male patients and typically with tens of participants at most, report peak glycine levels during or shortly after surgery and an apparent elimination half life on the order of tens of minutes. These data are sufficient to constrain the time scale of our audio envelopes, but far too sparse and population specific to support detailed compartmental modelling. Where this project draws on published glycine half life estimates from small intravenous studies in older male surgical patients (for example during transurethral resection of the prostate), these values are used only to set the time scale of the audio stimulus envelope on the correct order of magnitude, not to claim precise population kinetics. Serine shares aspects of the same nitric oxide centered thermoregulatory pathway and is discussed in the introduction for mechanistic context, but the present proof of concept work is restricted to glycine as the experimental molecule. No therapeutic claims are made for the audio or visual stimuli generated here; they are intended as non-chemical tools for future, ethically reviewed experiments.

2.2. Basis for the Vibrational Signature and Evaporation Sequence of Zwitterionic Glycine

2.2.1. Molecular Basis of the Vibrational Signature and Zwitterionic Glycine as the Reference Structure

Glycine (2 aminoacetic acid) is the simplest proteinogenic amino acid and exists predominantly in a zwitterionic form in aqueous and physiological environments, with a protonated amino group (NH3+) and a deprotonated carboxylate group (COO-). In the solid state and in solution its vibrational spectrum has been extensively characterized by infrared and Raman spectroscopy, supported by quantum chemical calculations [5–9]. The zwitterionic structure is therefore a natural reference for constructing a vibrational signature that can be mapped into sound.

In this work we treat zwitterionic glycine as the sole molecular template for the audio stimulus. Other metabolites and cofactors, including serine, are acknowledged in the introduction as part of the broader biochemical context but are not sonified. All vibrational information is taken from crystalline or solution phase glycine, using experimental IR and Raman datasets and, where necessary, quantum chemical calculations to fill in missing assignments [5–9]. This choice keeps the sonification tightly linked to one well defined molecular species.

2.2.2. Normal Modes and Frequencies

Within the harmonic approximation, the small amplitude vibrations of a molecule with N atoms can be decomposed into 3N minus 6 normal modes (3N minus 5 for linear molecules). Each normal mode Qi is associated with an angular frequency omega_i, a wavenumber v_i in cm-1, and an intensity in a given spectroscopic technique (for example IR absorbance or Raman scattering). For our purposes, the set of normal modes and their wavenumbers is taken from published normal mode analyses of zwitterionic glycine, rather than re derived from first principles.

Given a mass weighted Hessian H (the matrix of second derivatives of the potential energy with respect to mass weighted Cartesian coordinates), the normal modes and frequencies can be obtained by solving the eigenvalue problem

$$H\,L = L\,\Lambda$$

where L contains the eigenvectors (normal modes) and Lambda is a diagonal matrix of eigenvalues lambda_i. The harmonic angular frequencies are

$$\omega_i = \sqrt{\lambda_i}$$

and they relate to the wavenumbers and ordinary frequencies by

$$\tilde{\nu}_i = \omega_i / (2\pi c)$$

$$f_i = \omega_i / (2\pi) = c\,\tilde{\nu}_i$$

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where c is the speed of light expressed in cm per second for consistency with the spectroscopic literature. In practice we use reported wavenumbers v_i from IR and Raman studies of glycine as the primary input, and convert those to audio domain frequencies as described below.

2.2.3. Frequency mapPing from Molecular Vibration to Audio

Raw molecular vibrational frequencies lie in the terahertz range and are not directly audible. To create an audio representation we map each wavenumber v_i (in cm-1) to a corresponding audio frequency f_i_audio (in Hz) using a simple linear mapping

$$f\_i\_audio = a * v\_i + b$$

where a is a scaling factor in Hz * (cm-1)^-1 and b is an optional offset in Hz, usually set to 0 for clarity. A linear mapping preserves the relative spacing of modes and is easy to reproduce in other laboratories. In this project we adopt a mapping in which the prominent asymmetric carboxylate stretch around 1600 cm-1 corresponds to 300 Hz, resulting in

$$a = 300\ Hz / 1600\ cm\text{-}1$$

$$b = 0\ Hz$$

so that 1600 cm-1 -> 300 Hz, 3000 cm-1 -> approximately 562 Hz, and lower frequency skeletal modes map to proportionally lower audio frequencies. This choice keeps all mapped frequencies within a comfortable, low to mid audio band suitable for long listening without fatigue and avoids ultrasonic or very low sub audio components.

2.2.4. Mode Intensities and Per Mode Amplitudes

Each normal mode has an associated spectroscopic intensity that reflects how strongly it interacts with the electromagnetic field in a given technique. We treat these intensities as proxies for the relative loudness of the corresponding audio components. When both IR and Raman data are available for a given mode, a combined intensity I_i can be defined as a weighted sum

$$I\_i = w\_IR * I\_i\_IR + w\_Raman * I\_i\_Raman$$

where w_IR and w_Raman are scalar weights chosen to reflect the relative emphasis placed on each technique. For simplicity and reproducibility, we use equal weights unless a compelling reason exists to favor one dataset over the other. All intensities are normalized so that the sum over modes is equal to 1, and the initial audio amplitude A_i0 for each mode is proportional to this normalized intensity. This approach keeps the relative balance of partials faithful to the vibrational data rather than introducing arbitrary musical weighting.

2.2.5. From Molecular Spectrum to Audio Waveform

Given the mapped audio frequencies f_i_audio and initial amplitudes A_i0, the raw audio signal before any time dependent envelope is a sum of sinusoids

$$s(t) = sum\_i\ A\_i0 * sin(2\ pi\ f\_i\_audio\ t + phi\_i)$$

where phi_i are initial phases. In the primary stimulus we fix phi_i = 0 for all modes, which simplifies reproduction and keeps the focus on the amplitude envelope rather than on subtle phase interactions. In supplementary variants we allow phi_i to be randomized to create slightly different realizations with the same spectral content. In all cases, no new frequencies are introduced beyond those derived from the vibrational spectrum; the sound is a strict sum of molecularly anchored partials.

2.2.6. Grouping Modes by Chemical Motif

Although the primary pharmacokinetic stimulus applies a single global envelope to all modes, it is useful for interpretation and for the design of comparative stimuli to group modes by their dominant chemical motif. We therefore assign each mode to one of three broad groups based on its wavenumber region and published assignments:

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- Group A (NH3+ and CH2 “edges”): N H stretching modes in the 3000 to 3300 cm-1 range, CH2 stretches around 2900 to 3000 cm-1, and associated higher frequency deformations that carry much of the “edge” of the molecule.
- Group B (COO- and backbone): carboxylate asymmetric and symmetric stretches (approximately 1400 to 1700 cm-1), C N stretches, and mixed modes that define the zwitterionic backbone.
- Group C (skeletal and lattice): lower frequency modes below about 1200 cm-1, including skeletal deformations and lattice or collective motions in the solid.

These groupings are not used to assign different kinetics in the primary pharmacokinetic stimulus, but they underpin the design of the evaporation reference and the physiologically and clinically inspired exploratory envelopes described below.

2.3. Amplitude Envelopes: Pharmacokinetic Primary Stimulus and Evaporation Reference

2.3.1. Primary Pharmacokinetic Absorption Elimination Envelope

For the primary research stimulus we modulate all vibrational modes with a single global amplitude envelope E_PK(t) that is inspired by a simple one compartment oral pharmacokinetic model. In such models, the plasma concentration C(t) after an oral dose can often be approximated by the difference of two exponentials, representing absorption and elimination:

$$C(t) \text{ proportional to } \exp(-k_e * t) - \exp(-k_a * t)$$

where k_e is the elimination rate constant and k_a is the absorption rate constant, with k_a > k_e to allow a rise to a peak and then a decay. We adopt the same functional form for the audio envelope and write

$$E_{PK}(t) = C_{norm} * (\exp(-k_e * t_{phys}) - \exp(-k_a * t_{phys}))$$

where t_phys is a physiological time variable in seconds, C_norm is a normalization constant chosen so that the maximum of E_PK is 1, and k_e and k_a are chosen based on published glycine half life estimates. Specifically, we set

$$k_e = \ln(2) / t_{half}$$

with t_half on the order of 40 minutes based on small intravenous glycine studies in older male surgical patients, and choose k_a modestly larger than k_e so that the resulting concentration time curve peaks at approximately 1 hour in physiological time. This creates a physiologically plausible absorption elimination profile without overfitting scarce data.

To render a 5 minute audio file, we map the physiological time window of interest (for example 0 to 4 hours) onto the 0 to 300 second audio window using a constant compression factor

$$t_{phys} = alpha * t_{audio}$$

where t_audio runs from 0 to 300 seconds and alpha is chosen so that t_phys spans the desired number of hours. The audio amplitude applied to each mode is then

We chose a 0 to 4 hour physiological window for the envelope constraining E_PK(t), which spans the time during which glycine levels would be expected to rise, peak, and return toward baseline in the context of a single evening dose on the order of a few half lives, and overlaps the pre-sleep and early night intervals used in existing clinical trials [1–4], while remaining agnostic about compartment structure or individual variability [40]. The 5 minute duration of the rendered audio was selected as a pragmatic compromise: it is long enough for a clear rise and fall of the compressed pharmacokinetic envelope to be heard, yet short enough to fit within common 5 to 10 minute listening blocks used in psychophysiological and sleep related experimental protocols without undue fatigue [41].

$$A_i(t_{audio}) = A_{i0} * E_{PK}(t_{phys}(t_{audio})) * F_{tech}(t_{audio})$$

where F_tech(t_audio) is a short, purely technical fade in and fade out window applied at the start and end of the file to avoid digital clicks and abrupt transients; this is a standard practice in audio stimulus generation and has no physiological interpretation in the present work.

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2.3.2. Evaporation Reference Envelope (Four Stage Artistic Design)

In parallel with the pharmacokinetic envelope we construct an evaporation reference stimulus in which the relative contribution of the three motif groups changes over four qualitative stages:

1. Stage I ("sharp edges"): early dominance of Group A modes (NH3+ and CH2 stretches), conveying the exposed, high energy edges of the molecule.
2. Stage II ("structural identity"): increasing weight of Group B modes (COO- and backbone), representing the stable zwitterionic identity.
3. Stage III ("skeletal memory"): gradual shift toward Group C modes (low frequency skeletal and lattice motions), evoking a slower, heavier remainder.
4. Stage IV ("bath"): overall decay of all glycine modes into a low level residual field that can optionally be combined with a broad band thermal bath noise floor.

To implement this idea we assign group specific envelopes E_A(t_audio), E_B(t_audio), and E_C(t_audio) that are piecewise defined over the 0 to 300 second window. In Stage I (0 to T1), E_A(t_audio) rises rapidly from 0 to 1 with a short attack constant and then begins to decay, while E_B(t_audio) and E_C(t_audio) remain close to zero. In Stage II (T1 to T2), E_B(t_audio) is maintained near its maximum while E_A(t_audio) decays and E_C(t_audio) increases from a low baseline. In Stage III (T2 to T3), E_C(t_audio) decays with the longest time constant while E_A(t_audio) and E_B(t_audio) are near zero. In Stage IV (T3 to T_end), all three envelopes decay together so that only a low level residue remains before the final technical fade out.

Mathematically, each glycine mode i belonging to group g_i in {A, B, C} is assigned a time varying amplitude

$$A_i(t_{audio}) = A_{i0} * E_{group}(g_i, t_{audio}) * F_{tech}(t_{audio}),$$

where A_i0 is the static amplitude derived from the normalized vibrational intensity, E_group(g_i, t_audio) is the corresponding group envelope in the range 0 to 1, and F_tech(t_audio) is the short, purely technical fade described above. The stage boundaries T1, T2, and T3, the attack and decay time constants within each stage, and the relative maxima of E_A, E_B, and E_C were chosen to produce a continuous percept of "edges first, structure next, skeleton last" without abrupt jumps in loudness. Exact parameter values for the evaporation reference (T1, T2, T3 and per group time constants and scaling factors) are documented in the accompanying Python script for this stimulus so that other groups can reconstruct or modify the envelope explicitly.

We emphasize that the evaporation envelope is a chemically inspired artistic design: the choice of stage structure and time constants reflects an intuitive evaporation metaphor for zwitterionic glycine at an interface and is not fitted to empirical kinetic data. It is therefore provided as a clearly labelled reference stimulus for qualitative listening and hypothesis generation, not as the primary basis for quantitative claims.

2.4. Sigil Construction and Animation

The visual sigil for zwitterionic glycine was constructed as a concentric, time-evolving glyph that encodes the same vibrational groups used in the audio stimuli, so that spatial position and opacity carry information about frequency band and relative intensity [34,35]. The goal was to provide a stable, recognisable geometric "identity" for glycine that can be paired with the audio, rather than a literal depiction of molecular motion in vivo.

For each mode i with wavenumber nu_i (in cm^-1) and normalized intensity I_norm_i, the radius r_i of the corresponding ring element was defined as:

$$r_i = r_{min} + (r_{max} - r_{min}) * (nu_i - nu_{min}) / (nu_{max} - nu_{min})$$

where nu_min and nu_max are the minimum and maximum wavenumbers in the zwitterionic glycine spectrum. This linear mapping places the highest-frequency modes at the outer ring and lower-frequency modes nearer the center, preserving the qualitative idea that "sharper" modes live further from the origin while keeping all modes in a bounded visual field.

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Modes were grouped into functional classes analogous to those used in the audio envelopes [2,4]:

- Group A: NH3+/CH2 stretching region (nu_i >= 2900 cm^-1)
- Group B: COO-/backbone region (1200 cm^-1 <= nu_i < 2900 cm^-1)
- Group C: skeletal / low-frequency region (nu_i < 1200 cm^-1)

Each class was assigned a fixed quadrant center in polar angle to maintain a stable geometric identity across time, so that viewers can quickly learn which sector corresponds to which chemical motif [34]. Within each class, the individual modes were spread within that quadrant by small random angular offsets (jitter around the group center) to reduce overlap while preserving class cohesion.

Marker size was used to reflect relative normalized intensity. For each mode i we defined a symbol size size_i as:

size_i = size_min + (size_max - size_min) * (I_norm_i / I_norm_max)

with I_norm_max denoting the maximum normalized intensity across all modes. This mapping ensures that the visually dominant rings correspond to the strongest vibrational contributions, while lower-intensity modes remain visible but smaller. Radius and size remained fixed for each mode throughout the animation.

To mirror the 5 minute audio stimuli, the sigil animation used a total duration T_total = 300 seconds. Normalized time u was defined as:

u = t / T_total (0 <= u <= 1)

and each functional class was given a simple scalar opacity envelope G(u) analogous to the audio envelopes [35,36]:

- Group A (NH3+/CH2): A(u) = max(0, 1 - u / 0.4)
- Group B (COO-/backbone): B(u) = exp(- (u - 0.5)^2 / (2 * 0.15^2))
- Group C (skeletal): C(u) = min(max(0, (u - 0.2) / 0.4),

max(0, (1 - u) / 0.4))

At each animation frame f with time t_f, the opacity of mode i was set to:

alpha_i,f = alpha_max * G_i(u_f)

where G_i is A, B, or C according to the functional class of mode i. This construction makes NH3+/CH2 modes dominate early in the animation, COO-/backbone modes dominate near the middle, and skeletal modes dominate late, mirroring the qualitative “edges first, structure next, skeleton last” emphasis used in the evaporation reference audio while still remaining legible when paired with the pharmacokinetic stimulus.

To aid perception without changing the underlying mapping between radii and frequencies, all ring elements were rotated slowly about the center so that the sigil completed exactly one full rotation over 300 seconds:

omega = 2 * pi * N_rot / T_total

with N_rot = 1. The instantaneous angle of each mode was then:

theta_i,f = theta_i,0 + omega * t_f

while r_i and size_i remained constant. This rotation encourages the viewer to perceive the sigil as a single evolving object rather than a static diagram, and makes gradual changes in opacity easier to perceive over time [34].

The implementation was carried out in Python 3.14 using a standard plotting and animation library. The coordinates, radii, sizes, and opacity envelopes for all modes are generated directly from the same vibrational data and grouping rules used for the audio stimuli, and the complete scripts and parameter files for both the static sigil and the 5 minute animation are provided in the public code repository described in the Data and Code Availability section.

2.5. Audio and Video Generation and Playback Recommendations

All audio stimuli were generated with custom Python scripts implementing the vibrational mapping and envelope functions described above. Scripts were written in Python 3.14 using standard

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numerical and audio libraries, and are provided in full in the public code repository. For each stimulus, we rendered a 5 minute, dual mono WAV file at a sampling rate of 22 050 Hz and 16 bit integer depth. The initial sum of sinusoids was normalized to avoid clipping, with a target peak below 0.9 of full scale and a moderate root mean square level suitable for comfortable listening on typical laptop speakers.

Sigil animations were generated as sequences of still frames in a graphics environment and encoded into MP4 video files using ffmpeg with an H.264 codec. Frame rate was set to 8 frames per second, total duration to 300 seconds, and aspect ratio to a square 1:1 canvas with the sigil centered on a dark background. For each animation we created two versions: a vibrational only version in which the primary glycine audio stimulus is multiplexed as the audio track, and a narrated version in which a brief spoken explanation is overlaid on a lower level version of the same audio. The narrated version is intended to support visually impaired researchers and clinicians who may work with the stimuli.

All stimuli (audio only and audio plus sigil) were designed to be compatible with standard playback chains and to run on the native media player of common desktop and laptop operating systems. No specialized audio hardware is required. For consistency across sessions, we recommend that future experiments using these stimuli maintain a comfortable mid range playback volume, use the same playback device and loudspeaker position across conditions, and where possible avoid switching between headphones and speakers within the same protocol. In the original concept and in informal listening tests, we avoided headphones in order to minimize irregular high frequency energy directly at the head and instead favored chest level loudspeaker placement.

Audio and sigil generation: sampling rate, bit depth, duration, export format, and playback chain

Audio files

The primary vibrational stimulus used in this work is a 5 minute molecule derived audio file constructed from the zwitterionic glycine vibrational peak list described above. For the pharmacokinetic based stimulus, each audible partial corresponds to a single vibrational mode, and the global amplitude envelope follows a compressed 0 to 4 hour absorption elimination profile so that onset, peak, and decay can be explored within a 300 second window. A second, evaporation reference stimulus uses the same partials but applies group specific envelopes to emphasise different regions of the spectrum over time, providing a chemist inspired representation of a hypothetical evaporation sequence. Both stimuli were rendered with the same technical parameters to facilitate side by side comparison and reuse in future experiments.

All audio files were generated in Python 3.14 and exported with the following technical parameters:

- Sampling rate: 22,050 Hz
- Channels: stereo (dual mono; identical signal in left and right channels)
- Bit depth: 16 bit PCM (little endian)
- Total duration: 300 seconds (5:00)
- Amplitude: normalised to avoid clipping, with peaks below full scale and a moderate RMS level suitable for comfortable listening

The WAV files were written using a standard Python audio library, with internal floating point precision preserved until the final quantisation step. Within a given condition, no additional dynamic range compression, limiting, or equalisation was applied; differences between the pharmacokinetic primary stimulus and the evaporation reference stimulus arise solely from the distinct envelopes imposed on the same underlying set of partials.

Sigil video files

For each audio model we generated a matching sigil animation, yielding one video for the pharmacokinetic based stimulus and one for the evaporation reference stimulus. In both cases, each vibrational mode is represented as a point on a circular ring with radius proportional to wavenumber and brightness proportional to instantaneous envelope weight. The pharmacokinetic sigil applies a

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single global absorption elimination envelope and rotates the ring slowly over 5 minutes, whereas the evaporation sigil stages the relative brightness of mode clusters so that the outer “edge” modes become prominent early and then fade as lower frequency modes dominate.

Animations were rendered at 30 frames per second with a resolution of 1,920 x 1,080 pixels and encoded as H.264 MP4 files using ffmpeg. The audio track embedded in each MP4 is identical to the corresponding standalone WAV file, allowing researchers to use either audio only or audio plus sigil presentations without remixing.

Narrated versions for accessibility

In addition to the vibrational only videos, an optional narrated version was prepared in which a short spoken description of the stimulus and its intended use precedes the main sigil animation. This narrated track was created primarily for visually impaired or non technical listeners and for demonstration purposes. Narration audio was generated separately using text to speech, mixed to a lower background level than the vibrational stimulus, and combined with the video stream during encoding. No narration is included in the core stimuli recommended for sleep related experiments.

Playback chain

All stimuli (audio only WAV and MP4 video files) were designed to be compatible with standard consumer playback chains such as a laptop computer connected to a pair of near field loudspeakers or a compact desktop speaker. No specialised audio hardware is required; any device capable of playing 16 bit, 22,050 Hz stereo WAV or MP4 files without resampling will reproduce the stimuli with sufficient fidelity for initial laboratory piloting.

For consistency across sessions, users are encouraged to:

- Keep playback volume in a comfortable mid range (avoiding both near silence and sustained maximum output).
- Use the same playback device and loudspeaker position when comparing conditions (pharmacokinetic primary stimulus versus evaporation reference stimulus).

Headphone playback is technically possible, but was not used in the informal listening tests that motivated this prototype. Given the high frequency content of the stimuli and the potential for irregular head related filtering, we recommend chest level loudspeakers in a quiet room for sleep related protocols unless a specific headphone based design is being tested.

2.6. Ethics Statement

This work is based solely on previously published data and on computational and artistic transformations of molecular and clinical information. No new human or animal experiments were performed, and no identifiable participant data were accessed. The construction of audio and visual stimuli from published glycine spectra and trial summaries does not require individual consent. Any future use of the stimuli in human studies will require approval by an appropriate institutional review board or ethics committee and written informed consent from participants.

3. Results

3.1. Summary of Pre-Sleep Glycine Clinical Findings

Across published human studies, most pre-sleep glycine trials used oral doses around 3 g taken approximately 1 hour before bedtime and enrolled tens rather than hundreds of participants, with intervention periods ranging from a single night to several days [1–4]. Within this small evidence base, the most consistent pattern is a modest improvement in subjective sleep quality and next-day functioning in people with self-reported sleep complaints, together with relatively few adverse events.

In adults with chronic sleep complaints, nightly pre-sleep glycine has been reported to improve self rated sleep quality, reduce reports of fatigue and daytime sleepiness, and slightly improve performance on attention and memory tasks the following morning compared with placebo [3].

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Objective measures, where reported, tend to show small changes in sleep architecture rather than large shifts, and not all outcomes reach statistical significance.

In a separate study in which healthy volunteers were subjected to partial sleep restriction, pre-sleep glycine intake produced modest improvements in next-day performance and feelings of fatigue but did not fully normalize the impact of sleep loss [4]. Across studies, glycine was generally well tolerated, with no serious adverse events and only occasional mild gastrointestinal symptoms.

A focused narrative review by Bannai and Kawai summarized these trials and highlighted both the converging direction of effects and the limitations of the current literature [5]. Heterogeneous inclusion criteria, outcome measures, and dosing regimens, together with modest sample sizes and incomplete reporting of primary outcomes and core temperature measures, mean that estimates of effect size remain uncertain. In line with this assessment, the present work did not attempt a formal meta-analysis; instead, the clinical findings are treated as preliminary motivation for developing a transparent, molecule linked audio and visual prototype for future experiments.

3.2. Audio File Characteristics for Pharmacokinetic and Evaporation Reference Stimuli

Using the vibrational mapping and envelope framework defined in Section 2, we rendered two primary 5 minute audio stimuli from the same zwitterionic glycine spectrum. The first is a pharmacokinetic based stimulus in which all mapped modes share a single compressed absorption elimination envelope derived from published human half life estimates and constrained to a 0 to 4 hour physiological window before being mapped to 0 to 300 seconds of audio time. A companion stimulus is an evaporation reference stimulus in which the same modes are grouped into three functional classes and weighted by a four stage envelope that emphasizes edges first, structure next, and skeletal residue last as a chemist inspired metaphor for evaporation rather than a kinetic model.

In both stimuli, the spectrum is entirely determined by the zwitterionic normal modes and their relative intensities; no musical scales, chords, or additional harmonics are introduced during rendering. Dominant peaks in the audio correspond to the strongest vibrational bands, whereas weaker modes contribute low level components that fill in the sonic texture without changing its overall identity. This one to one mapping ensures that any difference between the pharmacokinetic and evaporation reference stimuli arises from their time varying amplitude envelopes rather than from different frequency content.

The pharmacokinetic stimulus rises smoothly from silence to a single broad maximum and then decays over the 5 minute window, mirroring the rise and fall of a simple one compartment concentration profile once compressed from physiological to audio time. In contrast, the evaporation reference stimulus begins with a sharper onset dominated by high frequency NH3+ and CH2 modes, passes through a middle phase in which COO- and backbone modes are most prominent, and ends with a long, low amplitude tail dominated by low frequency skeletal modes. Informal listening confirms that the pharmacokinetic stimulus is perceived as a single evolving block of sound with gradual breathing like dynamics, whereas the evaporation reference has a more stratified feel, with clearer transitions between early, middle, and late phases while still remaining continuous.

Both stimuli were rendered as 5 minute, dual mono WAV files at 22 050 Hz and 16 bit depth with conservative amplitude scaling to avoid digital clipping. The rendered waveforms show no discontinuities at onset or offset due to the application of a short technical fade in and fade out window, and spectrogram inspection confirms that no additional high frequency components or artefacts are introduced by the synthesis process beyond those implied by the vibrational mapping itself. The left and right channels are identical; no binaural beat or interaural phase offset protocol was used, and the stimuli are not designed as entertainment or beat based interventions.

3.3. Visual Sigil: Temporal Evolution

The visual sigil was constructed as a two dimensional geometric representation of zwitterionic glycine in which each vibrational mode is mapped to a ring element with radius proportional to its wavenumber and symbol size proportional to its normalized intensity, as described in Section 2.4.

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Modes belonging to NH3+/CH2, COO-/backbone, and skeletal regions are assigned to distinct angular sectors so that the overall sigil forms a stable, rotationally symmetric figure that can be animated over time.

To parallel the audio stimuli, we implemented simple opacity envelopes for each functional group and a slow rotation of the entire sigil over the 5 minute window. When the animation is driven by the pharmacokinetic envelope, all sectors brighten and fade together with a single broad maximum, preserving the overall geometry while producing a global rise and fall in apparent brightness. When the animation is driven by the evaporation style group envelopes, high frequency sectors appear more prominent early in the sequence, mid frequency sectors dominate in the middle portion, and low frequency sectors remain visible longest before fading, echoing the qualitative edges, structure, skeleton ordering used in the evaporation reference audio.

At any given time point, the positions and sizes of individual ring elements remain fixed; only their opacity and the global rotation angle change. This makes it straightforward to pair the sigil with either audio stimulus while maintaining a consistent visual identity for glycine. Taken together, the audio and sigil results provide two tightly coupled, fully specified non-chemical representations of the same molecule that are ready to be used as experimental stimuli in future studies, including protocols that compare responses to the pharmacokinetic stimulus, the evaporation reference, or their corresponding visual dynamics.

4. Discussion

4.1. Glycine as NO Linked Thermoregulatory Modulator

The present work was motivated by converging mechanistic and clinical observations that place glycine at the intersection of thermoregulation and sleep. Experimental studies in animals and humans suggest that pre-sleep glycine can modulate core body temperature and influence non rapid eye movement (NREM) sleep onset, potentially through enhancement of vasodilation and peripheral heat loss, together with central actions on thermoregulatory nuclei and sleep related networks [6–12]. Within this framework, oral glycine is understood less as a direct hypnotic and more as a permissive agent that improves the thermal and physiological conditions under which sleep can begin.

Human trials are broadly consistent with this mechanistic picture but remain modest in scale. Small randomized controlled studies in adults with self-reported sleep complaints suggest that 3 g of glycine taken before bedtime can improve subjective sleep quality and next-day fatigue, with limited changes in sleep architecture and core body temperature where measured [1–4]. A narrative review highlighted both the reproducible direction of effect and important gaps: heterogeneous inclusion criteria, differing outcome measures, short intervention periods, and incomplete reporting of thermoregulatory endpoints [5]. In line with that assessment, the present work does not claim to provide further evidence for clinical efficacy. Instead, the trial literature is used as a pragmatic starting point: it motivates the choice of glycine as a lead molecule and constrains the design of the audio stimulus to a plausible pre-sleep time window while explicitly acknowledging that quantitative effect sizes remain uncertain.

4.2. Audio Patterning as a Molecule-Anchored Physiological Bridge

The central question of this study is not whether glycine works as a sleep aid, but how a molecule centered audio and visual representation can be constructed so that it remains faithful to known chemistry and pharmacokinetics while still being usable as a practical stimulus in future experiments. Many existing approaches to “molecular music” or audio brain stimulation start from musical scales, binaural beats, or generic relaxation soundscapes and then layer biological interpretations on top [24–27]. In contrast, the present pipeline begins with the zwitterionic vibrational spectrum of glycine, maps those modes directly into the audio frequency domain, and only then applies simple amplitude envelopes derived from pharmacokinetic and chemist inspired considerations.

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Within this framework, glycine is treated as a test molecule for audio and visual tool design rather than as a uniquely privileged target. It was chosen because it is structurally simple with a well characterised zwitterionic form and compact vibrational spectrum, has randomized controlled trial evidence for pre-sleep ingestion, and is linked—through limited and heterogeneous data—to thermoregulation and subjective warmth.

Within this framework, the pharmacokinetic based audio stimulus is intentionally positioned as the primary, biologically conservative bridge. All mapped frequencies share a single absorption elimination envelope that is compressed from a 0 to 4 hour physiological window into a 0 to 300 second audio window, using published one compartment half life estimates as an order of magnitude guide rather than as precise predictors of individual concentration time profiles [16–21]. This yields a single broad rise and fall that parallels the expected pattern of glycine exposure after an evening dose, without implying that the audio waveform can reproduce blood levels or thermoregulatory dynamics in any literal sense. The mapping is therefore hypothesis driven but explicitly limited: it offers physiologically informed timing for an audio stimulus rather than a surrogate for pharmacokinetic measurement.

The evaporation reference stimulus is kept in a separate category. It uses the same vibrational modes and intensities but redistributes amplitude over time according to a four stage envelope that emphasizes high frequency "edge" modes early, backbone modes in the middle, and low frequency "skeletal" modes late. This construction reflects a chemist's intuition about surface loss and residue, and it was chosen because it produces a distinct yet recognizable listening experience. However, unlike the pharmacokinetic stimulus, the evaporation envelope is not anchored in empirical kinetic data, and the present work treats it as an artistically motivated reference rather than a biologically privileged pattern. The manuscript therefore offers both stimuli to future investigators but clearly separates the physiological rationale for the pharmacokinetic envelope from the more interpretive status of the evaporation sequence.

Importantly, both audio stimuli are rendered as dual mono waveforms: the left and right channels are identical, and no interaural frequency or phase differences are introduced. This makes the stimuli fundamentally different from binaural beat protocols or explicit entrainment paradigms that depend on interaural discrepancy to generate low frequency beat percepts [26,27]. Any physiological effects observed in future studies would need to be interpreted in terms of exposure to a molecule-anchored spectrum with slowly varying amplitude, rather than as a result of beat based frequency following responses.

4.3. Interpretation of Glycine Sonification and Sigil

The sonification and the visual sigil are best understood as two coordinated but distinct representations of the same underlying vibrational data. In the audio domain, each vibrational mode maps to a sinusoidal component at an audible frequency with amplitude determined by normalized intensity, and the choice of envelope determines how these components rise and fall over the 5 minute window. In the visual domain, the same modes are mapped to ring elements whose radii encode wavenumber, whose symbol sizes encode intensity, and whose angular positions group modes into functional sectors. The sigil animation then modulates opacity over time using envelopes that mirror either the pharmacokinetic pattern (global rise and fall) or the evaporation style group dynamics (edges, structure, skeleton).

For researchers and clinicians, the value of this dual representation lies not in proposing any special non physical property of glycine, but in making the mapping from chemical structure to stimulus space explicit and inspectable. Every ring in the sigil and every tone in the audio can be traced back to a specific vibrational mode, and the envelopes can be examined, critiqued, and replaced if desired. This transparency is particularly important in fields such as audio brain stimulation, where complex proprietary sound designs are sometimes presented as unitary interventions without a clear link to underlying physical parameters [24,28].

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At the same time, the qualitative differences between the pharmacokinetic and evaporation stimuli are not dismissed. Informal listening suggests that the pharmacokinetic audio is perceived as a single evolving block of sound with breathing like dynamics, whereas the evaporation reference feels more stratified, with clearer early, middle, and late phases. The sigil animations show analogous differences in the temporal pattern of group brightness. These contrasts are framed as starting points for hypothesis generation: they may suggest specific experimental contrasts (for example, comparing responses to pharmacokinetic versus evaporation stimuli), but they do not yet justify claims about differential efficacy.

4.4. Novelty and Positioning

Several aspects of the present work appear novel relative to the existing literature. First, to our knowledge this is the first fully specified pipeline that starts from a well characterized small molecule, uses its vibrational spectrum as the sole source of audio frequencies, and pairs a pharmacokinetic informed amplitude envelope with a parallel evaporation reference, both rendered as openly documented 5 minute stimuli. Previous studies have used molecular structures to inspire sound design or have applied generic binaural beat or isochronic tone protocols to sleep and anxiety, but have not combined a concrete thermoregulatory candidate, explicit pharmacokinetic modeling, and a reproducible audio mapping in this way [1–5,16–21,24–28].

Second, the work pairs audio with a geometric sigil that is constructed from the same vibrational data and uses the same grouping into functional classes. This cross modal design is positioned not as a decorative addition but as a tool for future experiments on audio-visual coupling, expectation, and recognition. The sigil can be used to standardize what participants see when they listen to the audio or to test whether learned visual familiarity with a molecule specific pattern modulates physiological or subjective responses to its sonification.

Third, the entire mapping is implemented in an open, script based form. All parameters needed to reconstruct the stimuli are provided, including the spectral data, grouping rules, envelope definitions, and rendering settings. This stands in contrast to “black box” interventions where only final audio files are shared. For laboratories operating under limited resources or strict standard operating procedures, this openness is intended to lower the barrier to adaptation: local teams can re-render or modify the stimuli while preserving a documented lineage back to the original vibrational and pharmacokinetic assumptions.

Finally, the manuscript deliberately avoids positioning the stimuli as established therapeutic tools. Instead, they are framed as a prototype designed to be biologically plausible, experimentally tractable, and transparent in its assumptions. This positioning is important both scientifically and ethically: it invites critical evaluation and replication rather than premature application as a clinical intervention.

4.5. Limitations

Several limitations must be acknowledged. First, the clinical literature that motivated the choice of glycine as a pre-sleep candidate remains narrow. Existing trials are small, often single center, and frequently omit detailed thermoregulatory measurements or long term follow up [1–5]. Meta analytic synthesis would therefore risk producing apparently precise but misleading estimates of effect size, and the present work instead treats the trials as preliminary context for a design exercise, not as a secure foundation for clinical recommendations.

Second, the pharmacokinetic model used to shape the primary audio envelope is intentionally simple. It does not incorporate multi compartment behavior, interindividual variability, or the influence of food, circadian phase, or comorbid conditions on glycine absorption and clearance [16–21]. The choice of a 0 to 4 hour window and a single compressed absorption elimination curve is a pragmatic compromise intended to keep the mapping interpretable, balancing the limited pharmacokinetic data available, the early night focus of existing pre-sleep glycine trials, and the need to obtain a smooth, clearly audible rise–peak–fall envelope within a 5 minute stimulus. As a result,

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the envelope should be viewed as a coarse, population level approximation rather than a subject specific prediction.

Third, although the evaporation reference stimulus is carefully defined and chemist inspired, its time course is not directly derived from measured physicochemical kinetics. The decision to emphasize certain functional groups early or late is a design choice, not a measured property of glycine solutions under evaporation in vivo or in vitro. The manuscript therefore treats any interpretation of the evaporation stimulus as hypothesis generating only.

Fourth, the present study does not report new physiological or behavioral data acquired with these stimuli. No sleep recordings, thermoregulatory measurements, or cognitive outcomes are presented; consequently, no claims can be made about efficacy, effect size, or clinical utility. All examples of potential applications remain speculative until tested in controlled experimental settings.

Fifth, audio delivery in real world contexts introduces additional sources of variability that are not addressed here. Differences in loudspeaker quality, room acoustics, listening posture, ambient noise, and individual hearing profiles can all alter the effective waveform that reaches the ear, even when the digital file is identical. The dual mono design avoids complications introduced by binaural beats but does not eliminate these practical considerations.

4.6. Future Research

Future work needs to move from conceptual design to empirical testing. A straightforward next step is a small, carefully controlled pilot study in which participants with self-reported sleep difficulties or experimentally induced partial sleep restriction listen to the pharmacokinetic stimulus, the evaporation reference, a spectrally matched but temporally scrambled control, or a silent control, before bedtime on different nights. Outcomes could include subjective sleep quality, next-day fatigue and cognitive performance, and, where feasible, simple measures of core or distal skin temperature. Such a study would not establish clinical efficacy but would provide the first direct test of whether these molecule-anchored stimuli have any measurable short-term physiological or behavioral effects.

A second line of research is comparative and extensible. The same pipeline could be applied to other small molecules with plausible roles in thermoregulation or sleep, using their own vibrational spectra and pharmacokinetic profiles to generate analogous audio and visual stimuli. This would allow researchers to test whether glycine is in any way special, or whether similar designs based on other compounds yield comparable responses. Comparative work could also examine whether participants can perceptually distinguish between different molecule specific stimuli and whether such discrimination relates to physiological responses.

Third, more sophisticated pharmacokinetic and physiologically based models could be integrated into the envelope design. For example, individualized envelopes could be generated from estimated clearance parameters, or multimodal models could link audio exposure, oral dosing, and core temperature dynamics within a single simulation framework. While this would increase complexity, it might also enable more targeted hypotheses, such as aligning the peak of the audio envelope with expected maximal vasodilation or with specific phases of the sleep onset process.

Finally, future studies will need to address ethical and translational considerations. If molecule-anchored audio stimuli are eventually shown to have reproducible effects on sleep or thermoregulation, questions will arise about appropriate clinical indications, integration with existing treatments, and communication to patients and the public. The present work does not attempt to answer those questions. Instead, it provides a transparent, fully specified starting point that can be adapted, tested, and, if necessary, completely revised in response to empirical evidence.

5. Conclusions

This work integrates biochemical, nutritional, clinical, and sonification perspectives to propose a transparent, molecule-anchored prototype for audio and visual stimuli derived from zwitterionic glycine. Glycine was selected as the lead molecule because of its dual role as a simple amino acid present in widely consumed foods and as a candidate modulator of thermoregulatory processes that

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influence sleep onset. Experimental and clinical data suggest that pre-sleep glycine can facilitate distal vasodilation, promote heat loss, and modestly improve subjective sleep quality in some individuals, although effect sizes are small and causal pathways remain incompletely characterized. In this context, glycine is treated not as a proven hypnotic but as a biologically plausible starting point for exploring molecule informed audio and visual interventions.

Human trials with 3 g of oral glycine before bedtime provide preliminary support for improved self-reported sleep quality and next-day functioning in adults with sleep complaints or partial sleep restriction, but they are limited by small sample sizes, short interventions, and incomplete thermoregulatory measurements. The present work does not attempt to replicate or extend these trials. Instead, the trial literature is used to constrain the design space: it motivates the focus on pre-sleep administration, frames a 0 to 4 hour physiological window as a reasonable target for envelope construction, and highlights the need for future studies that combine subjective outcomes with thermoregulatory and sleep architecture measures.

The project extends this picture into the vibrational domain by mapping glycine's zwitterionic vibrational spectrum into an audible range and using it to generate two complementary five minute audio stimuli. The pharmacokinetic based stimulus compresses a 0 to 4 hour absorption elimination window into a single smooth rise-peak-fall envelope that is applied uniformly across all mapped frequencies, using published one compartment half life estimates as order of magnitude guides rather than individual predictions. The evaporation reference stimulus uses the same set of frequencies and intensities but redistributes amplitude over time according to a four stage envelope that accentuates higher frequency "edge" modes early, backbone modes in the middle, and low frequency "skeletal" modes late, reflecting a chemist's intuition about surface loss and residue. Both stimuli are rendered as dual mono waveforms without interaural differences, distinguishing them from binaural beat or explicit entrainment protocols.

Within the broader landscape of audio brain stimulation, molecular music, and sleep interventions, this work occupies a deliberately cautious position. It does not claim that the glycine sonification or sigil has established therapeutic value, nor does it propose that audio exposure can substitute for pharmacological dosing or behavioral sleep therapies. Instead, it offers a fully specified pipeline that links vibrational data, envelope design, and rendering parameters in a form that can be inspected, critiqued, reproduced, and extended by other groups. The accompanying visual sigil, constructed from the same vibrational data and grouping rules, provides a parallel geometric representation that can be used to study audio-visual coupling, recognition, and expectation in future experiments.

In summary, the glycine sonification and sigil introduced here should be viewed as open, molecule-anchored prototypes that make their assumptions explicit rather than as finished interventions. They define a starting point for systematic experimentation on whether such stimuli have any measurable effects on thermoregulation, sleep, or related physiological and cognitive endpoints, and how those effects compare to conventional audio protocols. The most important next steps lie in carefully designed laboratory and clinical studies that test these stimuli against appropriate controls, quantify any observed effects, and feed those results back into the design of future molecule based audio-visual tools.

Data Availability Statement: All code, audio files, sigil videos, and narration text used in this work are archived as a citable, versioned snapshot on Zenodo (DOI: 10.5281/zenodo.17990315 (https://doi.org/10.5281/zenodo.17990315) and mirrored in the public GitHub repository at https://github.com/mm-abdalhamid/glycine-sonification-sleep. The Zenodo record corresponds to release V1.1.0 of the repository and contains the exact code and stimuli used to generate the figures and results described in this manuscript. Code is released under the MIT License; manuscript-style text and static figures are released under CC BY 4.0; audio and video stimuli (including sigil videos and narrated variants) are released under CC BY-NC 4.0. Any commercial use of the audio or video materials, or creation of derivative therapeutic or relaxation products, would require separate written permission from the corresponding author.

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Statement of Originality: The vibrational sonification of zwitterionic glycine and the corresponding animated sigil described in this manuscript are, to the best of the author's knowledge, original. In contrast to prior molecular music and binaural beat work, this project combines a pharmacokinetic informed amplitude envelope, an evaporation style reference envelope, and a geometric sigil built from the same vibrational data into a single, fully documented toolkit with openly available code and media. The conceptual framing, sonification pipeline, sigil design, and two model stimuli constitute a novel contribution that is intended to support and stimulate future experimental studies rather than to replace established clinical practice.

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