Systematic Field Theory of the RNA Glass Transition

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We prove that the Lässig-Wiese (LW) field theory for the freezing transition of the secondary structure of random RNA is renormalizable to all orders in perturbation theory. The proof relies on a formulation of the model in terms of random walks and on the use of the multilocal operator product expansion. Renormalizability allows us to work in the simpler scheme of open polymers, and to obtain the critical exponents at 2-loop order. It also allows us to prove some exact exponent identities, conjectured by LW.

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Together with DNA and proteins, RNA plays a key role in biology. As such it is important to understand their spatial conformations. While for proteins the lowest-energy fold depends strongly on the chemical constitution, and is only tractable numerically, the problem for RNA is simpler, due to a clear separation in energy scale between primary structure (the sequence), secondary structure (pairing of bases in a fold) and tertiary structure (embedding of a fold in 3D space). The homopolymer problem (all bases identical) was solved in 1968 by de Gennes [1]. He finds that the pairing probability of two RNA bases with labels s and t, counted along the backbone, scales like $\mathcal{P}(s,t) \sim |s-t|^{-\rho_0}$, with $\rho_0 = 3/2$. Real RNA molecules, however, consist of a sequence of four different bases, and their optimal fold depends on this sequence. Experimentally important (see, e.g., [2]) is further the observation, that pairings (s, t) and (s', t') are either nested ($s < s' < t' < t$) or independent ($s < t < s' < t'$), which graphically amounts to the rule to draw the sequence and the pairings on the plane without self-intersections (planarity). While the problem of a biological RNA sequence is best solved numerically, for reference it is crucial to understand the physics of (planar) pairings of a random sequence. This was pioneered by Bundschuh and Hwa [3]. They consider a random pairing model with partition function ($\beta = 1/k_B T$)

$$Z_\eta = \sum_\Phi \exp\Big[-\beta \sum_{1\le s<t\le L} \eta(s,t)\Phi(s,t)\Big], \qquad (1)$$

which is defined as a sum over all planar pairings Φ, such that $\Phi(s,t) = 1$ if (s, t) is a Watson-Crick pair, and 0 otherwise. The pair energy $\eta(s,t)$ is considered as a quenched Gaussian disorder variable $\eta(s,t)$, with

$$\overline{\eta(s,t)} = f, \qquad \overline{\eta(s,t)\eta(u,v)} - f^2 = \sigma^2 \delta(s-u)\delta(t-v).$$

This is an additional approximation from the model of a random sequence [4]. A key feature of the above model is a continuous freezing transition between a weak-disorder phase, at large scales undistinguishable from the homopolymer case, and a strong-disorder glass phase with nontrivial scaling, and of possible biological relevance since the conformation and properties of RNA depends on the sequence disorder, i.e., on the primary structure. This glass phase appears in the solution of [3] for (1) for the $n = 2$ replica case (instead of $n = 0$ relevant for the disordered case) and in numerical studies at strong disorder [3,5]. Although the initial model [3] is simple, RNA with strong disorder is highly nontrivial and quite difficult to study, making it a challenging problem.

In [6] Lässig and Wiese (LW) pioneered a field-theoretical approach for the transition to the glass phase. They showed their model to be renormalizable at first order in perturbation theory and calculated the critical exponents. Using a locking argument (see below), the scaling exponents for random RNA in the strong-disorder phase were derived, in good agreement with numerics [3,5].

It is important to understand if this approach is consistent, and if the estimates of [6] for the scaling exponents are reliable. Using a formulation of the LW model in terms of interacting random walks in $d = 3$ dimensions, and field theory tools developed for membranes [7,8] we show that the LW model is renormalizable to all orders. We also derive new scaling relations between exponents, and calculate critical exponents at second order.

The field theory of LW is defined through perturbation theory in the disorder strength $g_0 = \sigma^2$. One introduces n replicas, labeled by $\alpha = 1, \ldots, n$. Without disorder ($\sigma = 0$) the replicas are not coupled and the expectation value of a product of N contact operators $\Phi_\alpha(s_i, t_i)$ can be computed exactly. It describes the constrained configuration with N fixed pairings (s_i, t_i) $(i = 1, \ldots, N)$, i.e., $N + 1$ subrings of backbone length $\ell_0, \ldots, \ell_N$ (with $L = \ell_0 + \cdots + \ell_N$). As discussed above, this expectation value is

$$\langle \Phi_\alpha(s_1,t_1)\cdots\Phi_\alpha(s_N,t_N)\rangle_0 = \ell_0^{-\rho_0}\ell_1^{-\rho_0}\cdots\ell_N^{-\rho_0}, \qquad (2)$$

with $\rho_0 = \frac{3}{2}$ if the (s, t)'s form a planar pairing, and 0 otherwise. Since we are working with RNA strands of fixed length L, we are free to normalize the partition function of a single strand as $Z_0^{(n=1)} = \langle 1\rangle_0 = L^{-\rho_0}$.

The average over the disorder η generates an attractive interaction between each pair of replicas,

$$\mathcal{H}_i = -g_0 \sum_{\alpha<\beta} \iint_{1\le s<t\le L} \Psi_{\alpha\beta}(s,t), \tag{3}$$

with coupling $g_0 \propto \sigma^2$ and the overlap operator

$$\Psi_{\alpha\beta}(s,t) = \Phi_\alpha(s,t)\Phi_\beta(s,t). \tag{4}$$

The quenched disorder average is obtained for $n \to 0$. The averaged free energy $\bar{F}$ for a single strand is

$$\bar{F} = -\overline{\log Z[\eta]} = \lim_{n\to 0} -\frac{\partial}{\partial n} Z_n, \qquad Z_n = \langle e^{-\mathcal{H}_i}\rangle_0. \tag{5}$$

Similarly, the average $\bar{A}$ of an observable A is the $n \to 0$ limit of the average in the interacting theory. It is calculated as a perturbative series in the disorder strength g_0, and suffers from short-distance UV divergences. Taking ρ_0 as a regularization parameter, $\rho_0 \le 3/2$, LW show that these UV divergences are poles in $\epsilon = 2\rho_0 - 2$ at $\epsilon = 0$ and that the theory is 1-loop renormalizable at $\epsilon = 0$ ($\rho_0 = 1$). An UV-finite renormalized theory is defined through a renormalization of the disorder strength g_0 and of the backbone length L. At one loop, the renormalization-group β function for the disorder strength g gives a RNA freezing transition at $g = g^* > 0$ for $\epsilon > 0$, in particular, for the physical case $\epsilon = 1$, $n = 0$ [6].

Our goal is to construct a field theory which reproduces (2). For this we note that $\ell^{-\rho_0}$ is the return probability at proper time ℓ for a free random walk (RW) in $\mathbb{R}^d$ with $d = 2\rho_0$. Thus we introduce n independent RW's, $\mathbf{r}_\alpha$, $\alpha = 1,\ldots,n$ ($\mathbf{r}_\alpha(s) = \{r^\mu_\alpha(s); \mu = 1,\ldots,d\}$). To keep only planar pairings we use $n \times N$ pairs of auxiliary fields $\gamma^\alpha_a(s)$ and $\tilde{\gamma}^\alpha_a(s)$ ($a = 1,\ldots,N$), and study the limit $N \to \infty$, as in [9]. The free model is given by the action ($\dot{} := \partial/\partial s$)

$$\mathcal{S}_0 = \sum_{\alpha=1}^{n} \int_0^L ds \frac{1}{4}[\dot{\mathbf{r}}_\alpha(s)]^2 + \sum_{\alpha=1}^{n}\sum_{a=1}^{N} \int_0^L ds\, \tilde{\gamma}^\alpha_a(s)\dot{\gamma}^\alpha_a(s). \tag{6}$$

The propagators for r and γ, $\tilde{\gamma}$ are

$$\begin{aligned} \tfrac{1}{2}\langle [r^\mu_\alpha(s) - r^\nu_\beta(t)]^2\rangle_0 &= \delta_{\alpha\beta}\delta^{\mu\nu}|s-t| \\ \langle \tilde{\gamma}^\alpha_a(s)\gamma^\beta_b(t)\rangle_0 &= \delta^{\alpha\beta}\delta_{ab}\theta(t-s), \\ \langle \gamma\gamma\rangle = \langle \tilde{\gamma}\,\tilde{\gamma}\rangle &= 0, \end{aligned} \tag{7}$$

where $\theta(s) = 1$ if $s > 0$, and 0 otherwise.

The key point is that in the large-N limit, the observables for a strand of length L in the LW model correspond to the partition function for a closed RW in our model, with specific boundary conditions (the end points are fixed and there is a creation operator $\tilde{\gamma}$ at the origin and an annihilation operator γ at the end). The contact operator Φ changes to

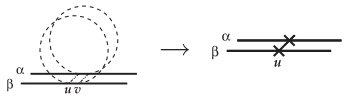
$$\Phi_\alpha(s,t) = \frac{1}{N}\sum_{a,b} \gamma^\alpha_a(s)\tilde{\gamma}^\alpha_b(s)\delta^d[\mathbf{r}_\alpha(s) - \mathbf{r}_\alpha(t)]\gamma^\alpha_b(t)\tilde{\gamma}^\alpha_a(t).$$

The pair-contact operator $\Psi_{\alpha\beta}(s,t)$ is still given by (4), and the interaction by (3). The auxiliary fields γ and $\tilde{\gamma}$ allow to select planar diagrams by taking $N \to \infty$. For the analysis of the UV-divergences, they are mere spectators. Their importance is that they allow one to write an action, and thus to apply established tools to prove renormalizability, and to obtain exponents at higher orders. For the sake of simplicity, we shall not write the γ's explicitly. We also note that a $\frac{1}{N}$ expansion is feasible, similar in spirit to [9] for the homopolymer problem.

The model defined by (6) belongs to a class of theories with multilocal interactions, including the Edwards model of polymers and self-avoiding manifolds [7,8]. Its short-distance singularities can be studied by the same multilocal operator product expansion (MOPE). Indeed, the operator Ψ is a product of bilocal operators $\delta[\mathbf{r}_\alpha(s) - \mathbf{r}_\alpha(t)]$ and of auxiliary fields $\gamma\tilde{\gamma}$. These auxiliary fields have a very simple propagator and a trivial short-distance expansion, which is a product of θ functions, multiplying the MOPE of the δ's. Let us give as examples the configurations which encode the UV singularities relevant at one loop. The short-distance behavior of a single Ψ is given by

$$\begin{aligned} \Psi_{\alpha\beta}(u,v) \underset{v\to u}{\simeq} |u-v|^{-d}\mathbf{1} \\ + |u-v|^{1-d}[\dot{\mathbf{r}}_\alpha(u)^2 + \dot{\mathbf{r}}_\beta(u)^2] + \cdots \end{aligned} \tag{8}$$

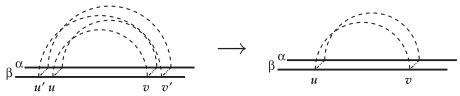
and is depicted graphically as



Similarly, two Ψ's can coalesce into a single Ψ in three ways. First, as already observed in [6]

$$\begin{aligned} \Psi_{\alpha\beta}(u,v)\Psi_{\alpha\beta}(u',v') \underset{u'\to u,v'\to v}{\simeq} C(u',u;v',v) \\ \times \Psi_{\alpha\beta}(u,v) + \cdots \end{aligned} \tag{9}$$

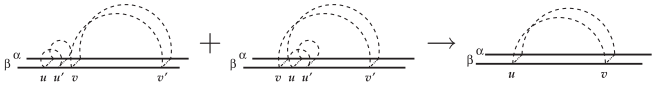
that we depict as



with $C(u',u;v',v) = (|u'-u| + |v'-v|)^{-d}$ the corresponding MOPE coefficient. Second, as

$$\Psi_{\alpha\beta}(u,u')\Psi_{\alpha\beta}(v,v') \underset{u\to v,u'\to v}{\simeq} D(u,u',v)\Psi_{\alpha\beta}(v,v') + \cdots \tag{10}$$

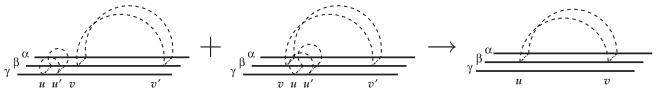
with $D(u,u',v) = |u'-u|^{-d}$ if $u < u' < v$ or $v < u < u'$, and $= 0$ otherwise, that we depict as



Third, as

$$\Psi_{\beta\gamma}(u,u')\Psi_{\alpha\beta}(v,v') \underset{u\to v,u'\to v}{\simeq} E(u,u',v)\Psi_{\alpha\beta}(v,v') + \cdots \tag{11}$$

with $E(u,u',v) = D(u,u',v)$, that we depict as



The perturbative expansion involves expectation values of integrals of products of Ψ operators. The short-distance contribution $u \to u'$ for a single $\Psi(u, u')$ in these integrals is given by (8) and produces an UV divergence. The first term in (8) gives a UV pole at $d = 1$ proportional to the insertion of the unit operator $\mathbf{1}$, while the second one gives a pole at $d = 2$ proportional to the operator $\dot{\mathbf{r}}^2$. Similarly, considering integrals involving two Ψ operators, the integrals over u and u' (v and v' fixed) in (9)–(11) give UV poles at $d = 2$, proportional to Ψ. In both cases, the subdominant terms in the MOPE involve higher-dimensional multilocal operators, but do not give any UV pole at $d \leq 2$. Note that although the left-hand side of (11) involves three replicas, the dominant term on the right-hand side involves only the 2-replica operator Ψ. (10) would not contribute for polymers or manifolds, since there is a third nonplanar diagram, and the sum of all cancel.

This analysis of the UV divergences through the MOPE at first order gives the same results as in LW. It shows that our model is renormalizable to one loop at $d = 2$, as expected from the existence of an action, and dimensional analysis. Our formulation and the MOPE allow to extend this analysis to all orders of perturbation theory [10]. The dimension $d = 2\rho_0$ is a dimensional regularization parameter, and short-distance UV divergences appear always as poles in $\epsilon = d - 2 = 2\rho_0 - 2$. We have shown that the theory is UV finite for $\epsilon < 0$ (apart from a trivial "vacuum energy divergence" proportional to the unity operator $\mathbf{1}$). For $\epsilon = 0$ the only UV divergences are proportional to the local operator $\dot{\mathbf{r}}_\alpha^2$ and to the bilocal operator $\Psi_{\alpha\beta}$ ($\alpha \neq \beta$). The MOPE also generates multilocal operators involving more than two replicas, for instance the three-replica operator $\Pi_{\alpha\beta\gamma} = \Phi_\alpha \Phi_\beta \Phi_\gamma$. However these operators are not associated to UV divergences, and correspond to irrelevant couplings. The crucial point in this analysis is that, since the interaction in the model involves two different replicas $\alpha \neq \beta$, no UV divergence appears which is proportional to the single-replica operator $\Phi_\alpha(u, v)$, although Φ is a "dangerously" marginal operator (it is marginal at $\epsilon = 0$ and relevant as soon as $\epsilon > 0$, like Ψ).

The renormalized UV finite theory is defined through the renormalized action $\mathcal{S}_R$

$$\mathcal{S}_R = \sum_\alpha \int_0^L ds \frac{\mathbb{Z}}{4} \dot{\mathbf{r}}_\alpha^2 + g_R \mu^{-\epsilon} \mathbb{Z}_g \sum_{\alpha<\beta} \iint_{0\leq u<v\leq L} \Psi_{\alpha\beta}(u, v) \qquad (12)$$

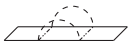
$\mathbb{Z}$ and $\mathbb{Z}_g$ are the wave-function and coupling-constant counterterms, and are series in g_R whose coefficients contain the poles in $1/\epsilon$. μ is the renormalization mass scale. The renormalized field $\mathbf{r}$ and coupling g_R are related to the bare ones $\mathbf{r}_B$ and g_B by $\mathbf{r}_B = \mathbb{Z}^{1/2}\mathbf{r}$ and $g_B = g_R \mathbb{Z}_g \mathbb{Z}^d \mu^{-\epsilon}$ (this differs from the LW scheme where s is renormalized instead of $\mathbf{r}$ and where $g'_B = g_R \mathbb{Z}_g \mathbb{Z}^2 \mu^{-\epsilon}$). The renormalization-group β function for the coupling, β_g, and the scaling dimension χ_r for the field $\mathbf{r}$ are

$$\beta_g = -\mu \frac{dg_R}{d\mu}\bigg|_{g_B}, \qquad \chi_r = \frac{1}{2}\left(1 + \beta_g \frac{d\log\mathbb{Z}}{dg}\right). \qquad (13)$$

Since we proved renormalizability, and identified all possible counterterms, we can simplify calculations by using open RWs instead of closed ones, eliminating the δ function for the closure. Although not all correlation functions are directly interpretable in terms of RNA strands, they are renormalized by the same counterterms, except for one additional boundary term $\mathbb{Z}_1$ for each end of the RW, $S_R^{\text{open}} = S_R^{\text{closed}} + 2\mathbb{Z}_1$. The (Fourier transformed) partition function $Z^{(1)}$ for a single free open RW then is

$$\text{——} = Z^{(1)}(\vec{q}) = \left\langle \prod_{\alpha=1}^{n} \mathrm{e}^{-\vec{q}(\vec{r}_\alpha(L) - \vec{r}(0))} \right\rangle = \mathrm{e}^{-n\vec{q}^2 L}. \qquad (14)$$

The first-order correction to (14) in the disorder strength is given by the following diagram



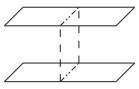
$$= g_0 \frac{n(n-1)}{2} \iint_{0<u<v<L} \mathrm{e}^{\vec{q}^2(2|v-u|-nL)} |v-u|^{-d}. \qquad (15)$$

Equation (15) is UV divergent when $u \to v$ (bulk) and u, $v \to 0$ or u, $v \to L$ (boundary). The corresponding UV pole in $\epsilon = 0$ has residue $(1 - 2L\vec{q}^2)\exp(-n\vec{q}^2 L)$. This partition function for a single open RW is renormalized as

$$Z_R^{(1)}(\vec{q}, g_R) = Z_B^{(1)}(\mathbb{Z}^{-1/2}\vec{q}, g_B) e^{-2\mathbb{Z}_1}. \qquad (16)$$

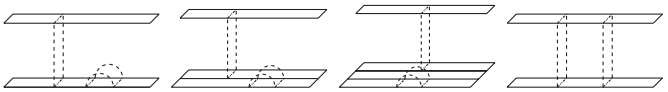
This implies that in the MS scheme the counterterms are at first-order $\mathbb{Z} = 1 + g_R(n-1)/\epsilon$, $\mathbb{Z}_1 = g_R(n-1)/4\epsilon$.

To compute $\mathbb{Z}_g$ it is simpler to consider the (connected) partition function $Z^{(2)}$ for two distinct interacting open RWs. At first order in g_0 it is given by



$$= Z^{(2)} = g_0 \frac{n(n-1)}{2} L^2 . \qquad (17)$$

At order g_0^2 there are four UV divergent diagrams, with MOPE given in (9)–(11),



and the corresponding function is renormalized as

$$Z_R^{(2)}(g_R) = \mathbb{Z}^{-d} Z_B^{(2)}(g_B) e^{-4\mathbb{Z}_1}. \qquad (18)$$

Care was taken to account for the (missing) zero-mode due to the δ distribution between the two replicas, resulting in the factor of $\mathbb{Z}^{-d}$. To subtract the UV pole at $\epsilon = 0$ the counterterm is $\mathbb{Z}_g = 1 + g_R(7 - 4n)/\epsilon$.

This scheme can be continued to 2-loop order [10]. To simplify the results we subtract minimally $\mathbb{Z}$ and $\mathbb{Z}_g\mathbb{Z}^d$. Also $\rho(g_R)$, the dimension of Φ, can be calculated by considering a 2-RW partition function Z_Φ with one Φ connecting the 2 RW's. We obtain at two loops:

$$\begin{aligned}\beta_g(g_R) &= -\epsilon g_R + (5-2n)g_R^2 + (3-2n)(5-2n)g_R^3\\ \chi_r(g_R) &= \frac{1}{2} - \frac{n-1}{2}g_R - \frac{(n-1)(4-3n)}{2}g_R^2 \qquad (19)\\ \rho(g_R) &= 1 + \frac{\epsilon}{2} + (n-1)g_R + \frac{(n-1)(3-4n)}{2}g_R^2.\end{aligned}$$

At one loop our results agree with those of LW [6], upon identifying $\beta = \beta_{\mathrm{LW}}$, and $\chi_r = 1/(2\gamma_{\mathrm{LW}})$. In the physical case of random RNA ($n = 0$), our 2-loop results confirm the existence of a UV fixed point (FP) (in our scheme at $g^* = \frac{1}{5}\epsilon - \frac{3}{25}\epsilon^2$), describing the freezing transition. The anomalous dimensions of Ψ and Φ at this FP are

$$\theta^* = \Delta_\psi(g^*) = 2 + \beta_g'(g^*) = 2 - \epsilon - \frac{3}{5}\epsilon^2 \qquad (20)$$

$$\rho^* = \Delta_\Phi(g^*) = 1 + \frac{3}{10}\epsilon + \frac{3}{50}\epsilon^2. \qquad (21)$$

On Fig. 1 we plot θ^* (black) and ρ^* (gray) from $\epsilon = 0$ to $\epsilon = 1$ (physical case). The full curves are our two-loop results, the dashed ones the one-loop estimates of [6]. The two-loop corrections do not change much the estimate for ρ^*, but do change it quantitatively for θ^*. Since $\Phi_\alpha(s,t) \le 1$, $\langle\Psi_{\alpha\beta}\rangle(s,t) \le \langle\Phi_\alpha(s,t)\rangle$ and thus $\rho \le \theta$. This bound is violated by our results for $\epsilon > \epsilon_c \simeq 0.59$. It is conjectured by LW that in this regime the two replicas are locked together, the exponent ρ in the glass phase equals the one at the transition, and that $\theta = \rho$. Finding a small ϵ^2 correction to ρ^* is important, since it validates the estimates of [6] for the exponents of random RNA. We find

$$\rho_{\mathrm{glass}} = \rho^*|_{\epsilon=1} \simeq 1.36, \qquad \zeta_{\mathrm{glass}} = 2 - \rho^* \simeq 0.64. \qquad (22)$$

Numerical results obtained by Krzakala *et al.* [5] in agreement with Bundschuh *et al.* [3,11] give

$$\rho_{\mathrm{glass}} \simeq 1.34 \pm 0.003, \qquad \zeta_{\mathrm{glass}} \simeq 0.67 \pm 0.02. \qquad (23)$$

The roughness exponent ζ is the dimension of the "height," i.e., the number of bonds to cross in order to get from 0 to r, $h(r) := \sum_{s<r}\sum_{t>r}\Phi(s,t) \sim r^\zeta$, with $\zeta = 2 - \rho$ [6]. The intrinsic fractal dimension of the branched "RNA-tree" is $d_f = 1/\zeta$. While in the molten phase $d_f = 2$, at the transition and in the glass phase $d_f \approx 1.5$. Steric effects are thus less important.

In [6] it was conjectured that the dimensions of Φ and $\mathbf{r}$ are related. To show an exact relation between χ_r and ρ, we remark that the partition function Z_Φ for one Φ connecting two strands is equivalent to that of two single strands, upon marking a single point on each strand, i.e.,

$$Z_\Phi = \frac{1}{n^2}\left[-\frac{\partial}{\partial q^2}Z^{(1)}(q)|_{q=0}\right]^2. \qquad (24)$$

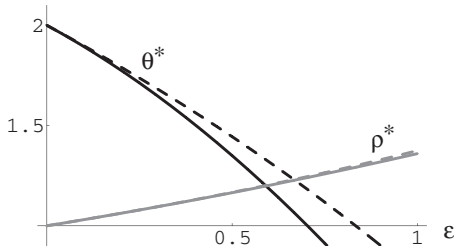


FIG. 1. Results for θ^* (black) and ρ^* (gray) at 1- (dashed) and 2-loop (solid) order.

At g^*, together with $\zeta + \rho = 2$ [6], this gives

$$\zeta^* = 2 - \rho^* = (2-\epsilon)\chi_r^*. \qquad (25)$$

To conclude, our results for the RNA freezing transition are as follows: Through a new field-theoretical formulation, we prove that the LW model [6] is renormalizable to all orders in perturbation theory, and the ϵ expansion well defined. We simplify the calculations by considering open RWs instead of closed ones. We perform the first 2-loop calculation for the critical exponents θ and ρ, and show that it does not much correct the LW estimate for ρ. Finally, we derive a new scaling relation between the height field h, and r. We also calculated the extension-force curve for the denaturation of random RNA under tension [12].

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