Journal of Statistical Physics, Vol. 119, Nos. 5/6, June 2005 (© 2005)
DOI: 10.1007/s10955-005-4408-z

Microscopic Models for Chemical Thermodynamics

V. A. Malyshev[1]

Received June 4, 2004; accepted March 7, 2005

We introduce an infinite particle system dynamics, which includes stochastic chemical kinetics models, the classical Kac model and free space movement. We study energy redistribution between two energy types (kinetic and chemical) in different time scales, similar to energy redistribution in the living cell. One example is considered in great detail, where the model provides main formulas of chemical thermodynamics.

KEY WORDS: Chemical thermodynamics; infinite particle systems; Kac model; chemical kinetics.

1. INTRODUCTION

As it is well known, thermodynamical functions and some formulas of the classical thermodynamics can be deduced from Gibbs canonical or grand canonical ensemble. However, all thermodynamics, even the heat exchange, has deeply dynamical nature and demands extra dynamics (this is even more true for the chemical thermodynamics). This extra dynamics can be modelled in various ways, satisfying however strong restrictins. For example, in some scaling limit for small time scales it should give thermodynamic formulas. In this paper, we give examples of such "thermo" dynamics, which, from one side, generalize the classical Kac(6) model (for convergence to Boltzman equation) and stochastic chemical kinetics processes (see refs. 11 and 18). From another side, it adds energy parameter to Streater's statistical dynamics(20) and Othmer's complex reaction networks theory.(5,19)

We try to concert this dynamics with the chemical thermodynamics and with energy redistribution between "heat" energy and chemical energy.

---

[1] INRIA, Rocquencourt, BP 105, 78153, Le Chesnay Cedex, France; e-mail: vadim.malyshev @inria.fr

We model this with two time scales. The first time scale corresponds to the "fast" dynamics, which governs the equilibrium behaviour, conserves the number of molecules of each type and brings the system quickly to equilibrium. In fact we assume that infinitely quickly. Second time scale corresponds to the "slow" dynamics, that does not conserve the number of particles, governs non-equilibrium process travelling along the manifold of equilibrium distributions. We model this dynamics with mean field dynamics of the stochastic chemical kinetics (taking into account energy redistribution).

We describe here the simplest possible case, which demonstrates conceptual picture without entering complicated mathematical techniques. Although the calculations in this paper do not meet any technical difficulties, it was not easy for me to reconstruct mathematically the conceptual picture corresponding to what is written in chemical textbooks. Obviously this model allows generalizations in many directions, including very technical. We discuss some of them in the last section.

The generalization of the Kac model goes roughly as follows. First, Kac type models (where a molecule possesses only kinetic energy, or velocity) are married with stochastic chemical kinetics, where normally the molecules differ only by type. As a result the molecule becomes characterized by a pair (j, T), that is by the type j and kinetic energy T. Then one more energy parameter is added to this pair—the chemical energy K. However, still there are no volume, pressure and other thermodynamic functions. Instead of introducing them apriori, "by hands", we throw particles independently into Λ and define the simplest possible but natural dynamics: velocities are defined by kinetic energies, and the particles move with constant velocities in-between the jumps.

The plan of the paper is the following. In Section 2 we define the model and show the existence of the limiting infinite particle dynamics, consisting of the free movement in space and some non-linear Markov process, corresponding to reactions. This dynamics, after some scaling limit, leaves invariant some manifold $\mathfrak{M}_0$ in the space of probability measures. This manifold is defined by finite number of parameters and consists of Gibbs equilibrium distributions for the mixture of ideal gases. We give selfcontained exposition of formulas for thermodynamic functions in Section 3. In Section 4 we introduce "thermo" dynamics (macroscopic evolution of thermodynamic parameters) and show that it is a deterministic dynamical system on $\mathfrak{M}_0$. In Section 5 we consider unimolecular reactions and chemical thermodynamics laws for this case. Last section is devoted to discussion of further problems.

I thank Christian Maes for kind attention, fruitful remarks and stimulating discussions.

2. MICRODYNAMICS

Molecules. We consider molecules as classical point particles with translational and internal (for example, rotational and/or vibrational) degrees of freedom. More exactly, first of all, any molecule is characterized by its type j. Translational degrees of freedom are given by its velocity $\vec{v} \in R^3$, coordinate $\vec{x} \in R^3$ and the kinetic energy $T_j = (m_j \vec{v}^2)/2$ (with mass m_j). Internal degrees of freedom are assumed to be of two kinds—fast and slow. They are also given by some energy functionals $I_j(y_j), K_j(z_j), y_j \in \mathbf{I}_j, z_j \in \mathbf{K}_j$ in the space $\mathbf{I}_j \times \mathbf{K}_j$ of internal degrees of freedom. It is often assumed (see ref. 9), that the total energy of the molecule is

$$E_j = T_j(v_j) + I_j(y_j) + K_j(z_j).$$

Thus, we assume that the degrees of freedom of the molecule can be "fast" or "slow". The corresponding parts of the energy will also be called either "fast" or "slow": T is always fast, and say I is fast, and K is slow. One of our goals is to introduce some models of energy redistribution between fast and slow parts.

For notation purpose only, we mostly take $I_j = 0$, unless otherwise stated, and we assume further on that $K_j = K_j(z_j)$ is constant, depending only on j. K_j can be thought roughly as the energy of some chemical bonds in the j type molecule.

Reactions. There are corresponding fast and slow reactions. Fast reactions do not touch slow parts, but slow reactions may change both slow and fast energies, thus providing energy redistribution between heat and chemical energy. We consider here the following reactions:

1. slow unary (unimolecular) reactions $A \to B$;
2. slow binary reactions of any type $A + B \to C + D$;
3. fast binary reactions of the type $A + B \to A + B$, which draw the system towards equilibrium;
4. fast process of heat exchange with the environment, with reactions of the type $A + B \to A + B$, but where one of the molecules is an outside molecule.

In any considered reaction the total energy conservation is assumed, that is the sum of total energies in the left side is equal to the sum of total energies in the right side of the reaction equation.

Now we proceed to rigorous definitions.

2.1. Finite Volume Dynamics

System in a finite volume Λ is defined as follows. Finite number N of particles (molecules) $i=1,\dots,N$, each equipped with degrees of freedom j,T,K, are thrown uniformly and independently in the cube Λ. The dynamics consists of two processes: basic Markov jump process $M_N(t)$, describing the evolution of internal degrees of freedom, and free space movement which will be defined for each trajectory of $M_N(t)$. The process $M_N(t)$ has states $\{(j_i,T_i), i=1,\dots,N\}$ and will be defined on the state space $\mathbb{I}=(\{1,\dots,J\}\times R_+)^N$. The particles in the process $M_N(t)$ are ordered, because in the space dynamics they will have coordinates.

Unary (unimolecular) reactions. Assume that $J(J-1)$ non-negative functions (rates)

$$u_{jj_1}=u_{jj_1}(T), \quad j\neq j_1$$

of $T\in R_+$ be given. Dependence on T is very important to be compatible with energy redistribution: for example, the reaction may not be possible for low reactant kinetic energies. The rates do not depend on i and are assumed bounded functions of T. Unimolecular reactions $A\to B$ have been used to describe many biological processes, for example, protein and RNA conformational transitions, transcription and translation processes etc.

Consider finite continuous time homogeneous Markov chain with state space $\mathbb{I}$, which is defined as follows: any particle i having at time t type $j=j(t)$ and kinetic energy $T=T(t)$ waits, independently of the other particles, some random time τ. This random time is assumed to have exponential distribution with the rate $u_j(T)=\sum_{j_1}u_{jj_1}(T)$. Then at time $t+\tau$ the particle chooses with probability $p_{jj_1}=(u_{jj_1}/\sum_{j_1}u_{jj_1})$ the type j_1 to perform the jump $j\to j_1$. However, the jump does occur iff $T+K_j-K_{j_1}\geqslant 0$. If $T+K_j-K_{j_1}<0$ then nothing occurs and the process starts anew.

One could equivalently say it like this. Define the allowed set

$$A(j,T)=\{j_1: T+K_j-K_{j_1}\geqslant 0\}$$

of types for the particle of type j and having kinetic energy T. Then such particle waits exponential time with the rate

$$u_j(T_i)=\sum_{j_1\in A(j,T)}u_{jj_1}(T_i)$$

and then changes its type to j_1 with probability

$$\frac{u_{jj_1}(T_i)}{\sum_{j_1\in A(j,T)} u_{jj_1}(T_i)}.$$

The transformation $j\to j_1$ of the particle i at time $t+\tau$ is accompanied by the energy redistribution $(T, K_j)\to(T_1 = T + K_j - K_{j_1}, K_{j_1})$. In other words, we assume energy conservation $T_1 + K_{j_1} = T + K_j$.

We also assume that the velocity v immediately after the jump $j\to j_1$ becomes uniformly distributed on the sphere of radius T_1. Note that one could assume much less.

We could define the state space of the process $M_N(t)$ as the sequence of arrays $X_i = \{j_i, \vec{v}_i\}, i = 1,\dots, N$. Then n_j is the number of i such that $j_i = j$, $N = n_1 + \cdots + n_J$. However, due to our agreement about velocities we can take instead the state of a molecule as $X_i = \{j_i, T_i\}$. Denote $H_N^{(u)}$ the generator of the N-particle process, defined on some appropriate function space on $(\{1,\dots, J\}\times R_+)^N$, which we will not write down explicitely, because it is quite standard.

For example for one particle we have continuous time Markov process $M_1(t)$ with the state space (j, T): the $T(t)$ component is uniquely defined by initial conditions and by the sequence of type transformations.

Slow binary reactions. Here the Markov jump process is the following. On the time interval $(t, t+dt)$ each (ordered) pair (i, i') of molecules, with parameters (j, T), (j', T') correspondingly, has a “collision” with probability $(1/N)b_{jj'}dt, b_{jj'} = b_{jj'}(T, T') = b_{j'j}$. Then at the moment of collision the parameters of the particles i, i' at time $t+0$ become correspondingly (j_1, T_1), (j_1', T_1'). The distribution of the new parameters is defined by the conditional densities

$$P^{(b)}(j_1, T_1, j_1'|(j, T), (j', T'))$$

that are defined for any $j, j', T, T', j_1, T_1, j_1'$, then $T_1' = T + K + T' + K' - K_1 - T_1 - K_1'$. To justify this definition it is assumed that

$$P^{(b)}(j_1, T_1, j_1'|(j, T), (j', T')) = 0$$

if $T + K + T' + K' - K_1 - T_1 - K_1' < 0$, and

$$P^{(b)}(j_1, T_1, j_1'|(j, T), (j', T'))\geqslant 0$$

if $T+K+T'+K'-K_1-T_1-K_1'\geqslant 0$. Moreover, for any $(j,T),(j',T')$

$$\sum_{j_1,j_1'}\int dT_1 P^{(b)}(j_1,T_1,j_1'|(j,T),(j',T'))=1.$$

We assume the same agreement about new velocities, that is each of them is distributed independently and uniformy on the corresponding energy sphere.

Denote $H_N^{(b)}$ the corresponding generator, on the same function space.

Fast binary reactions. Their definition is similar to slow binary reaction process, but the particles do not change types and slow energies, so only redistribution of their kinetic energies occurs, that is $T,T'\to T_1,T_1'$. The agreement concerning velocities holds as above. We write the collision probabilities as $(1/N)f_{jj'}\,dt$, $f_{jj'}=f_{j'j}$, we assume also that in the reaction $j,j'\to j,j'$ the energy conservation $T+T'=T_1+T_1'$ holds. We assume that $f_{jj'}$ do not depend on T and T'. As for the conditional distribution $P^{(f)}(T_1|T,T')$, we will use the one defined below, similar to the example in ref. 4.

We define Kac type models as follows. Assume that there is a family $M(a), 0\leqslant a<\infty$, of distributions μ_a on R_+ with the following property. Take two i.i.d. random variables ξ_1,ξ_2 with the distribution $M(a)$. Then their sum $\xi=\xi_1+\xi_2$ has distribution $M(2a)$. We assume also that a is the expectation of the distribution $M(a)$. Denote $p(\xi_1|\xi)$ the conditional density of ξ_1 given ξ, defined on the interval $[0,\xi]$. We put

$$P^{(f)}(T_1|T,T')=p(T_1|T+T')$$

and of course $T_1'=T+T'-T_1$. Denote the corresponding generator $H_N^{(f)}$.

Heat transfer. We model it similarly to the fast binary reactions, as random "collisions" with outside molecules in an infinite bath, which is kept at constant temperature β. The energy of each outside molecule is assumed to have χ^2 distribution with three degrees of freedom and with parameter β. More exactly, for each molecule i there is Poisson process with some rate h. Denote $t_{ik}, k=1,2,\ldots,$ its jump moments, when it undergoes collisions with outside molecules. At this moments the kinetic energy T of the molecule i is transformed as follows. The new kinetic energy T_1 after transformation is chosen correspondingly to conditional density p on the interval $[0,T+\xi_{ik}]$, where ξ_{ik} are i.i.d. random variables having χ^2 distribution with density $cx^{(1/2)}\exp(-\beta x)$. Denote the corresponding conditional density by $P^{(\beta)}(T_1|T)$. In fact, this process amounts to N independent one-particle processes, denote the corresponding generator $H_N^{(\beta)}$.

Full dynamics. Note that both for unary and slow binary reactions the numbers n_j of type j molecules are not conserved but the total number of molecules $N=\sum_j n_j$ is conserved. On the contrary, fast reactions conserve n_j. The process $M_N(t)$ is defined by the sum of generators

$$H(s_f, s_\beta)=H_N^{(u)}+H_N^{(b)}+s_f H_N^{(f)}+s_\beta H_N^{(\beta)}$$

on some appropriate function space on $(\{1,\dots,J\}\times R_+)^N$, where s_f, s_β are some large scaling factors, which eventually will tend to infinity. This process belongs to a class of well studied classical processes.

The state space of the full process is the sequence of arrays $X_i=\{j_i,\vec{x}_i,\vec{v}_i\}, i=1,\dots,N$, then n_j is the number of i such that $j_i=j$ molecules, $N=n_1+\cdots+n_J$. However, due to our agreement about velocities. we can take instead the state of a molecule as $X_i=\{j_i,\vec{x}_i,T_i\}$.

For each trajectory ω of $M_N(t)$ we define the local space dynamics as follows. It is quite simple: it does not change types, energies, velocities, but only coordinates. If at jump moment t the particle acquires velocity $\vec{v}(\omega)=\vec{v}(t+0,\omega)$ and has coordinate $\vec{x}(t,\omega)$, then at time $t+s$

$$\vec{x}(t+s,\omega)=\vec{x}(t,\omega)+\vec{v}(\omega)s \tag{1}$$

unless the next event (jump), concerning this particle, of the trajectory ω occurs on the time interval $[t,t+s]$. We assume periodic boundary conditions, or, that is the same, elastic reflection from the boundary.

We denote the resulting process $\mathfrak{X}_{\Lambda,N}(t)$. It depends of course also on the initial conditions and on s_f, s_β.

Remark 1. One of the disadvantages of the dynamics defined above is that there is no momentum conservation. This could be justified by including a fast process (similar to the defined above) of elastic collisions with some other smaller particles, which quickly establishes uniform distriution of velocities.[2] Moreover, instead of the motion with constant velocity in-between collisions in such models it could be even more natural to consider isotropic diffusion $w(t)$ with zero drift and put

$$\vec{x}(t+s,\omega)=\vec{x}(t,\omega)+w(s)$$

---

[2] The author thanks one of the referees for this remark.

instead of (1). Instead of the velocity $\vec{v}$ for one-particle motion one would have the covariance σ^2 of the diffusion. One should only fix somehow the dependence $T(\sigma^2)$. Most considerations below admit this generalization. Thus generalization could allow to take into account deeper results concerning reaction–diffusion equations, (see refs. 1, 2, 8 and 17).

2.2. Infinite Particle Dynamics

We show that the infinite particle limit exists. However, we do not get in general a Markov process, but only so called non-linear Markov process.

Unimolecular reactions. Denote $p_t(j,T), j=1,\dots,J$, the densities (with respect to the Lebesgue measure dT) of the one-particle process M_1 at time t

$$\sum_{j=1}^{J}\int p_t(j,T)\,dT=1.$$

If there are only slow unary reactions, then due to the energy conservation, for M_1 there exist (under mild conditions on u_{jj_1}) the limiting densities $\pi(j,T)=\lim_{t\to\infty} p_t(j,T)$, depending on the initial conditions, because this chain is strongly reducible.

Define infinite particle dynamics $\mathfrak{X}_{p_0}(t)$ as the collection of independent one-particle trajectories, where p_0 is the initial distribution for each particle. For infinite particle case one particle trajectories are defined exactly as in a finite volume, only there are no boundary conditions, and the particle moves in the whole space.

Define the limiting concentrations $c_j(t)=\lim_{\Lambda\to\infty}\Lambda^{-1}<n_j(t>=p_t(j)c$, where $p_t(j)$ is the probability that at time t a molecule has type j.

Heat transfer. Heat transfer is also a one-particle process and in the infinite particle evolution is defined similarly to the previous one. It will also be Markov.

Binary reactions. The case with binary reactions is more involved because one cannot define mean field dynamics directly for infinite particle system. Nevertheless, we define the so called non-linear Markov process. It consists of deterministic evolution of the densities $p_t(j,T)$, defined by some Boltzman type equation, and infinite number of independent inhomogeneous Markov jump processes for internal degrees of freedom of the individual particles. These two evolutions are concerted with each other in the sense we explain below. In this sense mean field dynamics in the infinite limit becomes local. In other words, if we are observing some local region, we never see simultaneous jumps of two particles, but only jumps of one particle—the particle with which it "collides" is a.s. infinitely far from this region.

The exact definition proceeds quite similarly to the finite particle dynamics with one essential difference. The infinite particle dynamics consists of the process $M_\infty(t)$ and free space movement. The jump process $M_\infty(t)$ is defined as collection of independent one-particle processes $M_{\infty,1}$. Each of this one-particle processes is defined by the following Kolmogorov equations:

$$\frac{\partial p_t(j_1,T_1)}{\partial t} = \sum_j \int (P(t;j_1,T_1|j,T)p_t(j,T) - P(t;j,T|j_1,T_1)p_t(j_1,T_1))dT \tag{2}$$

defining Markov process with distributions $p_t(j,T)$. To complete the definition one should define the transition kernel. When all four types of reactions are present, the kernel is

$$P(t;j_1,T_1|j,T) = \sum_{m=1}^{4} P^{(m)}(t;j_1,T_1|j,T) \tag{3}$$

that is the sum of four terms $m=1,2,3,4$, corresponding to the four reaction types, introduced above,

$$P^{(1)} = u_{jj_1}(T)\delta(T+K-K_1-T_1),$$

$$\begin{aligned} P^{(2)} &= \sum_{j',j'_1} \int dT'\,dT'_1 2b_{jj'}P^{(b)}(j_1,T_1,j'_1|(j,T),(j',T')) \\ &\quad p_t(j',T')\delta(T+K+T'+K'-K_1-T_1-K'_1-T'_1), \\ P^{(3)} &= \delta_{jj_1}\sum_{j'}\int P^{(f)}_{jj'}(T_1|T,T')2f_{jj'}p_t(j',T')dT', \\ P^{(4)} &= h\delta_{jj_1}P^{(\beta)}(T_1|T). \end{aligned}$$

We see that terms 2 and 3 depend on $p_t(j,T)$. One should find then $p_t(j,T)$ from equation, obtained by substituting (3) into (21). We get the

Boltzman type equation. In our case it is not difficult to prove existence and uniqueness of $p_t(j,T)$, because it is obtained as the limit of mean field processes. Also the chaos property similar to one in the Kac model follows. The chaos property corresponds to the independence of each particle jumps. Note however that the processes $M_{\infty,1}$ are time inhomogeneous.

Consider now infinite particle system in R^3, where each particle has internal parameters (j,v). Denote $\mathfrak{M}$ the system of all probability measures for this system with the following properties:

- coordinates of these particles are distributed as the homogeneous Poisson point field of particles on R^3 with some density c,
- each particle has a vector of parameters j,T distributed (independently of its coordinate and of the other particles) via some common distribution $p(j,T)$, the same for all particles.

Consider a sequence of processes $\mathfrak{X}_{\Lambda,N}(t)$ with $N=N(\Lambda)$, $\Lambda\to\infty$ so that $(N(\Lambda)/\Lambda)\to c>0$. Then at time 0 the distribution of $\mathfrak{X}_{\Lambda,N}(0)$ converges to some distribution belonging to the set $\mathfrak{M}$.

Theorem 2. If the initial distribution belongs to $\mathfrak{M}$ then the infinite-particle dynamics exists, moreover $\mathfrak{M}$ is invariant with respect to this infinite particle dynamics. Under the conditions stated above, the thermodynamic limit $\mathfrak{X}_c(t)$ of the processes $\mathfrak{X}_{\Lambda,N}(t)$ exists and belongs to $\mathfrak{M}$ at each time moment t.

Proof. To prove existence of the thermodynamic limit we proceed in two steps. On the first step we do not care about coordinates. If there are only unary reactions, there are no problem—one should not perform the thermodynamic limit. But for binary reactions one should.

Note that we can reformulate binary collisions in a finite volume as follows. As an example we take fast binary collisions where we can say that any particle i of type j undergoes "collision with SOME molecule of SOME type j'" with the probability

$$dt\sum_{j'}(f_{jj'}+f_{j'j})\frac{n_{j'}(t)}{N}.$$

After the infinite volume limit the probability of collision becomes

$$dt\sum_{j'}(f_{jj'}+f_{j'j})\frac{c_{j'}(t)}{c}. \tag{4}$$

The same can be done for the energy distribution, that is we get (2).

To prove the existence of infinite particle dynamics one should prove first the existence of solutions of the Boltzman equation, and then the existence of the Markov process for the individual particle. All these technicalities are put in Appendix A.

Remark 3. Note that in (4) one could interpret $c_{j'}(t)$ as some local concentration of particles in the vicinity of the j particle. This gives some links to local dynamics. This hints on some possible generalizations of the process which could include spatial correlations.

On the next step, we need to prove that the homogeneous Poisson distribution in space is invariant.

We use the following general lemma. Note that the assumption that the velocities are uniformly distributed on the energy sphere is not essential. It is sufficient only that the velocity process did not depend on the coordinates.

Lemma 4. Let all particles in the configuration $\{x_i(t)\}$ in R^d move (independently) as

$$x_i(t) = x_i(0) + \int v_i(s, \omega) ds,$$

where the velocities $v_i(t, \omega)$ are independent processes with arbitrary time dependence. Then the Poisson distribution is invariant.

Proof. Take N such particles in the finite cube Λ with the same independent movement, only take periodic boundary conditions. The result will follow if we prove that the uniform distribution on Λ^N is conserved with such dynamics. In fact, one can perform afterwards the thermodynamic limit with $(N/\Lambda) \to c$. Then the uniform distribution at any time t converges to the Poisson distribution, the finite volume dynamics at time t converges to the dynamics in R^d because for fixed t and sufficiently large Λ the particle does not reach the boundary of Λ. Thus Poisson distribution is invariant. See also general results of this kind in ref. 3.

Because of the independence it is sufficient to consider $N = 1$ that is one particle, thrown at time 0 with uniform distribution into Λ. Assume that the particle moves in this cube with some speed $v(t)$—arbitrary random function of time. The only condition is that $v(t)$ does not depend on the coordinate of the particle. Then it is clear that the uniform distribution is invariant.

3. THERMODYNAMIC FUNCTIONS FOR MIXTURE OF IDEAL GASES

In our case the Gibbs state will be the system of independent particles (ideal gas). Here we give a selfcontained presentation (fixing the notation we use here) of main formulas for the classical ideal gases and mixtures, with one important difference: the fast degrees of freedom are gaussian and slow degrees of freedom are constants K_j, depending only on j.

A well-known example of internal energy functional is the quadratic Hamiltonian

$$I_j = \sum_{k=1}^{d_j-3} \frac{m_{j,k} w_{j,k}^2}{2},$$

where $m_{j,k}, k = 1, \ldots, d_j - 3$, are some coefficients and the vector $y_j = \{w_{j,k}, k = 1, \ldots, d_j - 3\} \in R^{d_j-3}$. Then $d_j - 3$ is the number of internal degrees of freedom of the molecule of type j, d_j is the number of all degrees of freedom. This is justified, for example, when internal oscillations are small, (see ref. 9). We will call this the Gaussian case. We will need another extreme case, when K_j are constants.

Thus each molecule of type j has the energy

$$E_j = T_j + I_j + K_j.$$

We consider a finite number n_j of particles of types $j = 1, \ldots, J$ in a finite volume Λ. For the ideal gas of the j type particles the grand partition function of the Gibbs distribution is

$$\begin{aligned}
\Theta(j, \beta) &= \sum_{n_j=0}^{\infty} \frac{1}{n_j!} \left(\prod_{i=1}^{n_j} \int_{\Lambda} \int_{R^3} \int_{\mathbf{I}_j} d\vec{x}_{j,i}\, d\vec{v}_{j,i}\, dy_{j.i} \right) \\
&\quad \times \exp \beta(\mu_j n_j - \sum_{i=1}^{n_j} (\frac{m_j v_{j,i}^2}{2} + I_j(y_{j,i})) - K_j) \\
&= \sum_{n_j=0}^{\infty} \frac{1}{n_j!} \Lambda^{n_j} \beta^{-(d_j/2)n_j} B_j^{n_j} \exp \beta(\mu_j - K_j) n_j \\
&= \exp(\Lambda \beta_j^{-(d_j/2)} B_j \exp \beta_j \hat{\mu}_j),
\end{aligned}$$

where

$$B_j = \left(\frac{2\pi}{m_j}\right)^{(3/2)} \prod_{k=1}^{d_j-3} \left(\frac{2\pi}{m_{j,k}}\right)^{(1/2)}, \quad \hat{\mu}_j = \mu_j - K_j.$$

General mixture distribution of J types is defined by the following partition function:

$$\Theta = \prod_{j=1}^{J} \Theta(j,\beta) = \exp(\Lambda \sum_j \lambda_j \exp \beta\hat{\mu}_j), \lambda_j = \beta^{-(d_j/2)} B_j.$$

Define the grand thermodynamic potential

$$\Omega = \Omega_\Lambda = -\beta^{-1} \ln \Theta = -\beta^{-1} \Lambda \sum_j \lambda_j \exp \beta\hat{\mu}_j.$$

The limiting space distribution of type j particles is the Poisson distribution with rate (concentration) c_j, and

$$c_j = \frac{<n_j>_\Lambda}{\Lambda} = \beta^{-1} \frac{\partial \ln \Theta}{\partial \mu_j} = \lambda_j \exp \beta\hat{\mu}_j = \exp(\beta\mu_j - \beta\mu_{j,0} - \beta K_j).$$

Put $c = c_1 + \cdots + c_J$. Then

$$\mu_j = \beta^{-1} \ln\left(\frac{<n_j>}{\Lambda} \lambda_j^{-1}\right) = \mu_{j,0} + \beta^{-1} \ln c_j + K_j, \tag{5}$$

where

$$\mu_{j,0} = -\beta^{-1} \ln \lambda_j = -\beta^{-1}\left(-\frac{d_j}{2} \ln \beta + \ln B_j\right) \tag{6}$$

is the so-called standard chemical potential, it corresponds to the unit concentration $c_j = 1$.

The internal energy in thermodynamics is defined as the mean of the sum of energies of all particles. The conditional mean energy (given type j) particle is (the law of equipartition of energy)

$$< E_j > = \frac{d_j}{2} \beta^{-1} + K_j$$

and

$$U=\sum_j <n_j> \left(\frac{d_j}{2}\beta^{-1}+K_j\right).$$

The pressure is defined as

$$P=-\frac{\partial\Omega}{\partial\Lambda}=\Lambda^{-1}\beta^{-1}\sum_j <n_j>=\beta^{-1}\sum_j c_j=\sum_j p_j,$$

where $p_j=\beta^{-1}c_j$ are the partial pressures. In the thermodynamic limit this is equivalent to the definition

$$\beta P=\lim_{V\to\infty}\frac{1}{\Lambda}\ln\Theta.$$

The well-known equation of state follows:

$$P\Lambda=\beta^{-1}\sum_j <n_j>. \tag{7}$$

For one type j the entropy is defined as

$$S_j=-\frac{\partial\Omega_j}{\partial(\beta^{-1})}=\Lambda\lambda_j\ \exp(\beta\hat{\mu}_j)\left(\frac{d_j}{2}+1-\beta\hat{\mu}_j\right)=<n_j>\left(\frac{d_j}{2}+1+\beta K_j-\beta\mu_j\right).$$

(Sackur–Tetrode formula). For the mixture it is the sum of these $S=\sum_j S_j$.

Together with the internal energy U three other important thermodynamic potentials are: the enthalpy

$$H=U+P\Lambda=\beta^{-1}\sum_j <n_j>\left(\frac{d_j}{2}+1+\beta K_j\right). \tag{8}$$

Gibbs free energy

$$G=H-\beta^{-1}S=\sum_j \mu_j <n_j>$$

and Helmholtz free energy

$$F = U - \beta^{-1} S.$$

We can define also the densities of the extensive (that is asymptotically linear in Λ) thermodynamic variables in the thermodynamic limit. For example, we define the limiting Gibbs free energy for unit volume as

$$g = \lim_{\Lambda \to \infty} \frac{G}{\Lambda} = \sum \mu_j c_j.$$

4. "THERMO" DYNAMICS

For given rate parameters u, b, f, h the internal degrees of freedom of the particles are independent and identically distributed random variables. In other words, the distribution belongs to $\mathfrak{M}$. However, the kinetic energies may have not χ^2 distributions, that is the velocities may not have Maxwell distribution. We will force the kinetic energies to become χ^2 using the limit $s_f \to \infty$.

Denote Gibbs state of the j-type ideal gas as $\mathcal{G}_j = \mathcal{G}_j(\beta, \mu_j)$. Define $\mathfrak{M}_0 \subset \mathfrak{M}$ the set of all measures $\times_j \mathcal{G}_j(\beta, \mu_j)$ for any $\beta, \mu_1, \dots, \mu_J$, and $\mathfrak{M}_{0,\beta}$—its subset with fixed β. In physical and biological books on non-equilibrium thermodynamics, there are some general statements, (see for example, ref. 21), which hold for many concrete examples, in particular they will hold in our model. First, there is a submanifold in the space of probability measures on the state space, defined by a finite number of macroparameters, and moreover, this submanifold is invariant with respect to the full dynamics. Second, each point of this manifold is a product of k independent measures. In our case each point $\nu \in \mathfrak{M}_0$ is a product $\nu = \nu_1 \times \cdots \times \nu_J$ and the points of $\mathfrak{M}_0$ are in one-to-one with the vector $\mathcal{M} = (\beta, \mu_1, \dots, \mu_J)$ of parameters. Note that a point of $\mathfrak{M}_0$ is also uniquely defined by the vector $(\beta, c_1, \dots, c_J)$. The third general statement concerns different time scales, that we discussed above.

The following result, in despite of its evidence, is crucial for discussing chemical thermodynamics.

Theorem 5. The limits in distribution

$$\mathfrak{C}_c(t) = \lim_{s_f \to \infty} \mathfrak{X}_c(t), \mathfrak{D}_{c,\beta}(t) = \lim_{s_h \to \infty} \mathfrak{C}_c(t)$$

exist for any fixed t. Moreover, the manifold $\mathfrak{M}_0$ is invariant with respect to the process $\mathfrak{C}_c(t)$ for any fixed rates u, b, h. The manifolds $\mathfrak{M}_{0,\beta}$ are invariant with respect to $\mathfrak{D}_{c,\beta}(t)$.

Thus, in the process $\mathfrak{C}_c(t)$ the velocities have Maxwell distribution at any time moment. For the process $\mathfrak{D}_{c,\beta}(t)$ moreover, at any time t the temperature is equal to β, that is there is heat exchange with the environment.

The resulting process $\mathfrak{C}_c(t)$ on $\mathfrak{M}_0$ can be defined, using the evolution of $c_j(t)$ and formula (5), also by the deterministic evolution of the vector $\mathcal{M}(t) = (\beta(t), \mu_1(t), \dots, \mu_J(t))$

5. THERMODYNAMICS OF UNIMOLECULAR REACTIONS

Let us make first some remarks about conserved quantities. Note that $N = \sum_j < n_j >$ (for finite Λ) and $\sum_j c_j$ (for inifinite volume) are conserved. Then from the equation of state (7) it follows that the pressure P is conserved (for fixed β), the same for the grand potential. Thus in our model N, P, Λ are conserved.

Further on we consider only the process $\mathfrak{D}_{c,\beta}(t)$. Then all thermodynamic potentials are functions (for fixed $K_1, \dots, K_J$) on $\mathfrak{M}_{0\beta}$, for example the enthalpy H, or the Gibbs free energy G.

Hess's law. Consider two different processes $\mu_j^{(1)}(t)$ and $\mu_j^{(2)}(t), j = 1, \dots, J$, on $\mathfrak{M}_{0,\beta}$, for example with different reaction rates. Assume also that for some $T > 0$

$$\mu_j^{(1)}(0) = \mu_j^{(2)}(0), \mu_j^{(1)}(T) = \mu_j^{(2)}(T), \quad j = 1, \dots, J$$

that is these two processes have the same initial and final points. Then the Hess law says that the differences between initial and final enthalpies are the same for both processes. In fact, this law holds automatically in our model, because both processes are described by two paths on $\mathfrak{M}_{0,\beta}$ with the same initial and final points, and the enthalpy is a function on the invariant manifold $\mathfrak{M}_{0,\beta}$.

The simplest classification of reactions is in terms of the enthalpy H. If $\Delta H = H(\infty) - H(0) < 0$ then the reaction is called exothermic, the heat Q is goes to the environment, if $\Delta H > 0$ the reaction is endothermic and the heat is taken from the environment. That is $\Delta H = Q$.

Equilibrium conditions. We assume further on that there are no slow binary reactions, moreover we consider the case $J = 2$. That is, consider the system with two types and two reversible reactions $1 \rightleftarrows 2$. Thus we have 2 parameters μ_1, μ_2 and fixed β.

Let us remind how[7] the equilibrium condition $\mu_1 = \mu_2$ appears in chemical thermodynamics. For the extensive variable $X = < n_1 >$ the corresponding conjugate variable A (thermodynamic force) is (assuming $N = < n_1 > + < n_2 >$ fixed) called (chemical) affinity

$$A = -\frac{\partial G}{\partial X}|_{\beta,P,N} = -\mu_1 + \mu_2 = -\Delta G_0 - \beta^{-1} \ln \frac{c_1}{c_2},$$
$$\Delta G_0 = \mu_{1,0} - \mu_{2,0} - (K_1 + K_2)$$

ΔG_0 is called the free energy of the reaction. Note that instead of vectors $(\mu_1, \dots, \mu_J)$ for the points of $\mathfrak{M}_{0,\beta}$ one can use points $(c_1, \dots, c_J)$. Then A can also be defined as

$$A = -\frac{\partial g}{\partial c_1}|\beta, P, c.$$

The equation of state (relation between X and A) is

$$c_1 = \frac{c}{1 + \exp(-\beta A - \Delta G_0)}.$$

Equilibrium points are defined as points where $A = 0$, this gives $\mu_1 = \mu_2$. From (5) it follows that the equilibrium condition $\mu_1 = \mu_2$ in chemical thermodynamics uniquely defines the quotient $(c_{1,e}/c_{2,e})$ of the equilibrium densities $c_{j,e}$. The equilibrium constant is defined as

$$\kappa = \frac{c_{1,e}}{c_{2,e}} = \exp(-\beta \Delta G_0). \tag{9}$$

Moreover, for a given c the equilibrium condition uniquely defines a (fixed) point on $\mathfrak{M}_{0,\beta}$, that is the invariant Gibbs measure.

Stochastic chemical kinetics reconstructed. Now we give an example of such process in our case. Assume $K_1 < K_2$. Assume now the simplest possible dependence of $u_{jj'}$ on T: $u_{jj'}(T)$ equal some constants $w_{jj'}$ if $T_j + K_j - K_{j'} \geqslant 0$, and $u_{jj'}(T) = 0$ otherwise. Then the process $\mathfrak{O}_{c,\beta}(t)$ can be given explicitely. Denote $g_\beta(r) = P(|\xi| > r)$ for the χ^2 random variable ξ with inverse temperature β.

It is easy to see that the process $\mathfrak{O}_{c,\beta}(t)$ can be reduced to the Markov chain on $\{1, 2\}$ with rates

$$v_{21} = w_{21}, \quad v_{12} = g_\beta(K_2 - K_1) w_{12}.$$

Monotonicity of Gibbs energy for fixed β. This law says that Gibbs free energy G has its minimum at the fixed point and $G(t)$ is monotonic in time. It is evident in the vicinity of the equilibrium point. One can say more, if the process $c_j(t)$ corresponds to some Markov process.

Let any Markov process with two states $1, 2$ be given such that for some constant C

$$p_1(t)=Cc_1(t),\, p_2(t)=Cc_2(t), \quad \pi_1=Cc_{1,e},\ \ \pi_2=Cc_{2,e}, \tag{10}$$

where $p_j(t)$ are its probabilities at time t, and π_j are its stationary probabilities.

Remind that for a finite irreducible Markov chain with the rates $w_{jj'}$ the entropy of the positive measure $p=(p_1,\dots,p_J)$ relative to the stationary measure $\pi=(\pi_1,\dots,\pi_J)$ is defined as

$$S_M=\sum p_j \ln\frac{p_j}{\pi_j}=C\sum c_j \ln\frac{c_j}{c_{j,e}}. \tag{11}$$

Now we will prove that the Gibbs free energy g and Markov entropy S_M are equal up to a multiplicative and additive constants.

Theorem 6. At any time t we have for the Gibbs free energy density $g(t)$

$$g(t)=\mu c+\frac{1}{\beta C}S_M(t),$$

where $\mu=\mu_1=\mu_2$. It follows that $g(t)$ is time monotone.

Moreover, the process $p_j(t)$, satisfying (10), is unique, up to a common time scale.

Proof. For the Gibbs free energy density we get using (5)

$$\begin{aligned} g &= \lim_{\Lambda}\frac{G}{\Lambda}=\sum_j c_j\mu_j=\beta^{-1}\sum_j c_j \ln c_j+\sum_j c_j(\mu_{j,0}+K_j)\\ &=\beta^{-1}\sum_j c_j\ln c_j+\sum_j c_j(\mu-\beta^{-1}\ln c_{j,e})=\mu c+\beta^{-1}\sum_j c_j\ln\frac{c_j}{c_{j,e}}. \end{aligned} \tag{12}$$

At the same time

$$S_M=\sum p_j \ln\frac{p_j}{\pi_j}=C\sum c_j \ln\frac{c_j}{c_{j,e}}.$$

As S_M is known to decrease during Markov evolution, (see ref. 12), the second assertion of the theorem follows as well.

Let us show now that there is unique choice of dynamics, that is of the rates $v_{jj'}$, which give equilibrium condition $\mu_1 = \mu_2$. Each Markov chain with two state is reversible, because reversibility condition $\pi_1 v_{12} = \pi_2 v_{21}$ follows immediately from Kolmogorov equation

$$\frac{d\pi_1}{dt} = \pi_2 v_{21} - \pi_1 v_{12}.$$

Then

$$\frac{\pi_1}{\pi_2} = \frac{c_{1,e}}{c_{2,e}}. \tag{13}$$

In fact from

$$\frac{\pi_1}{\pi_2} = \frac{v_{21}}{v_{12}}$$

and (13) it follows that $v_{jj'}$ are uniquely defined up to some constant C, which determines some common time scale (speed of both reactions) and is irrelevant to thermodynamics. Theorem is proved.

Relation with Onsager theory in our example is the following. The flux is defined as

$$J_1 = \dot{X}_1$$

or in the thermodynamic limit

$$J_1 = \frac{dc_1}{dt}.$$

And from the equations

$$\frac{dc_1}{dt} = c_2 u_{21} - c_1 u_{12}, c_2 = c - c_1$$

we have

$$J_1 = \frac{1 - \exp(-\beta A)}{u_{21}^{-1} + u_{12}^{-1} \exp(-\beta A)}.$$

Energy redistribution. Assume that at time $t = 0$ an arbitrary distribution $p_0(j, T)$ of the vector (j, T) is given. Then at any $t > 0$ the densities $p_t(j, T)$ for any particle will be

$$c\sqrt{T}\exp(-\beta T) p_t(j) \tag{14}$$

for some $p_t(j)$. This can be shown as follows. As the internal degrees of freedom of infinite number of particles are i.i.d. random variables, then there exist a.s. the limits

$$\bar{T}(t) = \lim_{\Lambda\to\infty} \frac{1}{\Lambda} \sum_{i:x_i\in\Lambda} T_i(t), \bar{K}(t) = \lim_{\Lambda\to\infty} \frac{1}{\Lambda} \sum_{i:x_i\in\Lambda} K_{j_i}(t)$$

exist at any time t. In particular, a.s. for any fixed values of $K_{j_i}(t)$ the limits

$$\bar{T}(t) = \lim_{\Lambda\to\infty} \frac{1}{\Lambda} \sum_{i:x_i\in\Lambda} T_i(t, \vec{K}(t))$$

exist and are equal. Here $\vec{K}(t) = \{K_{j_i}(t), i = 1, 2, \dots\}$.

Moreover for any given $\vec{K}(t)$ there is a sequence of jump moments

$$t_1 < t_2 < \cdots < t_n < \cdots$$

of fast binary collisions and heat transfer, which do not change parameters j_i (and thus K_{j_i}) of the molecules. If s_f and s_β. tend to infinity we have a.s. there will be "infinite" number of fast collisions and heat transfers between any two unary reactions. It follows that any time t we have a product measure (14).

We will study the sequence $\bar{K}(t)$. As any time moment $t \geqslant 0$ we have $\bar{T}(t) = \beta^{-1}$ put also $\bar{T}(0) = \beta^{-1}$ for continuity. Now there two possibilities:

1. $\bar{K}(0) < \bar{K}(\infty)$, this means that the kinetic energy, pumped up to the system with the heat, is transformed to the chemical energy;
2. $\bar{K}(0) > \bar{K}(\infty)$, this means that the chemical energy is transformed to the kinetic energy, which goes out as the heat.

6. FURTHER PROBLEMS

This paper is a kind of advertisement for mixed dynamics. Pure local dynamics, even in one dimension, leads immediately to too difficult problems. Mixed dynamics is simpler and many situations could be modelled with it, especially in biology. It is quite natural to discuss here possible related problems, there are many.

Logical structure. From one side, chemical thermodynamics has some distinct logical structure, from the other side this structure is based on some approximations. Our model suggests a distinct implementation of this logical picture, and shows what is the nature of the approximations. Moreover, there are fundamental questions. We go now to more detailed discussion:

- Chemical thermodynamics largely uses ideal gas formulas (for example see formula (5)). For this reason the corresponding expressions can be only approximate;

- Equilibrium conditions play the central role in the chemical kinetics. In fact, they are based on the assumption that the chemical equilibrium corresponds to the minimum of the Gibbs free energy, in a sufficiently large class of measures, see the end of this section. It is not at all clear for me whether this should be considered as a fundamental experimental fact or it should be deduced from microscopic dynamics. A possible key could be the coincidence of some thermodynamic potential with Lyapounov function for the dynamics, see the above example (see also refs. 13 and 10);

- The dynamics for a system with chemical reactions is ambiguous itself. The reactions can be incorporated into hamiltonian dynamics only via some probabilistic mechanism. It is what we do here, using another field of physical chemistry—stochastic chemical kinetics. This dynamics cannot be arbitrary—the constraints on it are posed by the equilibrium conditions, given apriori.

- There is also a deeper reason for the dynamics ambiguity. If we do not want to use random mechanisms for reaction, we are encountered with the dual nature of bound states. From one side, bound states are considered (in chemical thermodynamics) as fundamental particles at EACH (except discrete time moments when reactions occur) time moment. From the other side, it appears as a composite particle (in the classical physics) from hamiltonian dynamics via scattering theory. In the latter for the bound state formation one needs INFINITE or at least finite time interval. Thus, it is ambiguous to prescribe when the new composite particle appears.

- The same problems arise for quantum hamiltonians with chemical reactions, in terms of annihilation-creation operators, with non-quadratic terms corresponding to collisions.

- Possibly there is some escape from all these problems even in the general local models, that is for nonideal gases with interaction between different gases. There should be equivalent representation of this complex system by ideal gases of quasiparticles. The corresponding quasiparticles could even correspond to real particles surrounded with clouds, that is the particles become slightly renormalized. However, quasiparticle representation can be obtained now rigorously only for some ground state models, and only for equilibrium dynamics (see ref. 10). This approach brings us to another *tabula rasa*: consider an infinite particle system where elementary particles are atoms, not molecules. Then we are in the framework of purely Hamiltonian system. One should be able to show that the dynamics brings this measure to the configurations where most atoms form bound states—molecules.

Non ideal systems. The deterministic part of the theory of chemical networks is presented in ref. 19, in completely rigorous beautiful framework. However, there was no energy component, no probability and no microscopic dynamics.

The logical framework of ref. 19 is the following: deterministic chemical kinetics is postulated together with some restrictions on the invariant manifolds, related to the (also postulated) Gibbs free energy G. It is presented as

$$\frac{\partial G}{\partial c_j} = \mu_j = \mu_{j,0}(\beta, P) + \beta^{-1} \ln \gamma_j(c)c_j,$$

where $\gamma_j(c_j)$ are some unknown functions of c_j. If $\gamma_j(c_j) = c^{-1}$ for all j, then the system is called ideal. As for the non-ideal systems, microscopic models should give information about γ_j.

However, even for non-ideal system the same question as above will be the main enigma of the chemical thermodynamics.

More thermodynamical processes. We did not consider chemical thermodynamics for binary reactions in this paper. However, it is clear that it can be done, because (as it is shown in Section 2) its inifinite particle dynamics is quite similar to unimolecular dynamics. Also reactions which do not conserve N are of interest. In particular, decay and synthesis that is $A \to B + C$ and $A + B \to C$. Here for the first reaction one should assign somehow the coordinate to B and C. It can be done in the following way:

one molecule, for example B, with probability (1/2) will have the coordinate of A, then C is put randomly into Λ. It seems unnatural in a finite volume, but in the infinite volume, it will give, as for slow binary reaction, a local process for particles. Together with evolution of densities.

We are lacking microscopic models even for simpler situations in non-equilibrium thermodynamics: local models quickly become too difficult to be useful. However, mixture of local models with mean field dynamics looks quite promising, and tractable. For example, one could consider exchange of matter with the environment, work and efficiency produced by mechanochemical and chemochemical machines, etc. (see ref. 14).

In quantum case there can be other statistics, Fermi and Bose, reactions with them are interesting to consider. Also one could try to model reactions in solutions or reactions with large P, nuclear reactions, etc. Some substitutes for Clausius entropy are used in nuclear physics, for which there are no dynamical models.

Biology. In biology it is known heuristically that the chemical networks may have different time scales. First scale is the fundamental micro-scale, it is the fastest scale, where local equilibrium establishes for some thermodynamic parameters (for our model it was the global equilibrium). Second scale (call it micro non-equilibrium), is the scale of main concrete reactions.

If the chemical network is large enough there can be also other scales, even slower than the second one. For example, genetic networks can be modelled as if the list of reactions changes with time, slower than the scale of the reactions.

It seems very important to understand and classify these scales and model all main time scales. One cannot yet even pose exact mathematically reasonable questions here.

Variational problems. Assume that some system has states $1, 2, \dots$ with energy levels ε_k of the state k. Gibbs distribution on the set $\{1, 2, \dots\}$ is defined as

$$p_k = Z^{-1}\exp(-\beta\varepsilon_k), \quad Z = \sum_k \exp(-\beta\varepsilon_k).$$

Then it is known and easy to show that Gibbs equilibrium state is the state of maximum entropy S for fixed mean energy U. To see this we are looking for extrema of

$$S = -\sum_k p_k \ln p_k + \lambda \sum_k \varepsilon_k p_k$$

with two constraints

$$U=\sum_k \varepsilon_k p_k = c, \quad \sum_k p_k = 1.$$

Thus we are looking for extrema of

$$-\sum_k p_k \ln p_k + \lambda \sum_k \varepsilon_k p_k + \gamma \sum_k p_k.$$

Differentiation gives

$$-\ln\, p_k + 1 + \lambda\varepsilon_k + \gamma = 0.$$

That is

$$p_k = C \exp \lambda\varepsilon_k,$$

where $\lambda < 0$ for convergence reason.

Similarly, equilibrium state is the state of minimum mean energy U for fixed entropy S. Here we differentiate

$$U + \lambda S + \gamma \sum_k p_k = \sum_k \varepsilon_k p_k - \lambda \sum_k p_k \ln\, p_k + \gamma \sum_k p_k.$$

Grand canonical ensemble is included to the previous scheme. In fact, consider grand canonical ensemble

$$\sum_{N=0}^{\infty} \exp \beta((\mu N - \sum_{k=1}^{\infty} \varepsilon_{Nk}),$$

where ε_{Nk} are the energies levels of the system with N particles. This case can be reduced to the previous one if μN is considered among the energy levels, that is introduce $\varepsilon_{N0} = -\mu N$.

The Helmholtz free energy $A = U - \beta^{-1} S$ is defined for any measure, that is for any system $\{p_k, \varepsilon_k\}$. In our case P and Λ are constant, as

$$P = \beta^{-1} c.$$

Thus the Gibbs free energy $G = A + P\Lambda$ is also defined for some class of measures, including our manifold $\mathfrak{M}_0$. It could be interesting to know the widest class of measures, where G is defined and is a Lyapounov function for an appropriate "thermo" dynamics.

APPENDIX A

Here we present some technicalities omitted in the main part of the paper. We use here natural and intuitive, but "not quite standard", approach to the convergence proof of mean field type Markov processes with large number of particles. It does not use standard techniques of martingale problem, semigroup generators, tightness of measures, etc, as for example in Ref. 16. This approach, coming from cluster expansion ideas, is based on small piece of combinatorics and simple probabilistic estimates. To avoid cumbersome notation, we present this method for binary reactions only, that is general enough to see all peculiarities. Moreover, it is clear that this approach can be applied to many other situations as well. This techniques proves both smooth dependence of the limiting distributions on t and on initial data, and the chaos property.

The model. Consider continuous time Markov process $\xi^N(t)=(\xi^N_v(t), v=1,\dots,N), t\in[0,\infty)$ with state space S^N, where S is some space of one-particle states. To define the process we fix some linear operator $U\colon M(S^2)\to M(S^2)$, where $M(S^2)$ is the set of measures on S^2 with variation norm. This operator is defined by the conditional measures $d\sigma(s_1,s'_1|s,s')$, where $d\sigma$ is the family, indexed by the pairs (s,s'), of probability measures on the set of pairs (s_1,s'_1). For any pairs v,v' of different particles the operators $U(v,v')$ define transformations on the set $M(S^N)$ of measures on the state space S^N. This operator acts as U only on v and v' components of S^N, it is assumed symmetric with respect to permutation $v\leftrightarrow v'$.

The transitions of the process are defined in two steps. First, each particle $v=1,\dots,N$ generates independent Poisson process of time moments with rate λ. Denote $N_v=N_v(\omega)$ the random number of time moments on the time interval $[0,t]$, generated by the particle v and let

$$0<t_{v,1}(\omega)<\cdots<t_{v,N_v(\omega)}(\omega)<t$$

be the these moments. We have

$$P(N_v(\omega)=n)=\frac{(\lambda t)^n}{n!}\exp(-\lambda t)$$

and the density of the vector $(t_1<\cdots<t_n)$ is given by

$$\begin{aligned}
&p(t_1<\cdots<t_n)dt_1\dots dt_n\\
&\quad=\exp(-\lambda t_1)\lambda\,dt_1\dots\exp(-\lambda(t_n-t_{n-1}))\lambda\,dt_n\exp(-\lambda(t-t_n))\\
&\quad=\exp(-\lambda t)\lambda^n\,dt_1\dots dt_n.
\end{aligned}$$

In other words, it is uniform on the simplex $\{0 < t_1 < \cdots < t_n < t\}$. At each time moment $t_{v.i}$ a pair (v, w_i) is produced, where $w_i \neq v$ is chosen with probabiity $1/(N-1)$. One could say equivalently that each pair generates independent Poisson process with rate $2\lambda/(N-1)$. Merging them together, we get the combined Poisson process, which we denote

$$0 < t_1(\omega) < t_2(\omega) < \cdots < t_n(\omega) < t.$$

It has rate (density) $N\lambda$.

For a given ω denote $v(i,\omega), v'(i,\omega)$ the pair produced at time t_i in the combined process. In fact, we can take ω as the sequence

$$(t_i, v_i, v_i'), \quad i = 1, 2, \ldots \tag{15}$$

itself.

We will consider (ordered) sequences of (unordered) pairs

$$\theta = (v_1, w_1), \ldots, (v_n, w_n). \tag{16}$$

We call $|\theta| = n$ the length of θ. Thus for any ω the sequence

$$\theta = \theta(\omega) = ((v_i, v_i'), i = 1, 2, \ldots)$$

is defined.

For any sequence θ we define the chronological product of measure transformations

$$U(\theta) = U(v_n, w_n) \ldots U(v_1, w_1)$$

acting from left to right. Thus, for any ω the quantities $\theta(\omega), n = n(\omega)$ and $U(\omega) = U(\theta(\omega))$ are uniquely defined. The measure on S^N at time t is given by

$$\mu^N(t) = \int U(\theta(\omega)) d^N \omega,$$

where $d^N \omega$ is the measure on Poisson trajectories for given N.

Assume, for any N, that at time $t = 0$ the one-particle distributions $\mu_v(0)$ of s_v are i.i.d. Then we have the following result.

Theorem. For any $v = 1, 2, \ldots$ one-particle measures $\mu_v^N(t)$, converge as $N \to \infty$ uniformly in $\mu_v(0)$ on any finite interval $(0, \tau_0)$, to some $\mu_v(t)$, identical for any v. Moreover, k-particle distributions $\mu_{1,\ldots,k}^N(t)$ converge to the product $\mu_1(t) \times \cdots \times \mu_1(t)$.

The plan of the proof will be the following. For τ_0 sufficiently small we will obtain explicit absolutely convergent series for any finite-dimensional distribution. This gives complete control for small times. To prove the same properties for larger t one can use the semigroup property (as one can write $t = k\tau_0 + t'$ for some k and $t' < \tau_0$) and uniformness on the initial one-particle distribution.

Clusters. We need some combinatorics. We call abstract sequence (16) of pairs connected if $V_k \bigcap \{v_k, w_k\} \neq \varnothing$ for any $k = 1, \ldots, n-1$, where

$$V_k = \bigcup_{i=k+1}^{n} \{v_i, w_i\}.$$

The pair $\{v_i, w_i\}$ in θ is called essential if $\{v_i, w_i\}$ does not belong to V_i. Connected sequence is called essential if all its pairs are essential. It follows that there are no identical pairs in the essential connected sequence. We call w-sequence any connected sequence with $w \in \{v_n, w_n\}$.

For any v and any ω we define a subsequence $\theta_v(\omega)$ of $\theta(\omega)$ as follows. Take maximal j such that $v \in \left\{v_j, w_j\right\}$. If there is no such j then put $\theta_v(\omega) = \varnothing$. If there is such $j = j(\omega)$ then we define $\theta_v(\omega)$ as the minimal subsequence of $\theta(\omega)$ satisfying the following two conditions: (1) if $v \in \{v_i, w_i\}$ then $\{v_i, w_i\} \in \theta_v(\omega)$; (2) if for $i \leqslant j$ the pair $\{v_i, w_i\}$ belongs to $\theta_v(\omega)$, then any pair $\{v_k, w_k\}$ for $k < i$ and such that $\{v_i, w_i\} \cap \{v_k, w_k\} \neq \varnothing$, also belongs to $\theta_v(\omega)$.

Resummation formula. For given v and any connected v-sequence θ we consider the probabilities

$$P^N(\theta) = P(\theta_v(\omega) = \theta), \; P_k^N = \sum_{|\theta| = k} P^N(\theta)$$

and will use the following resummation formula:

$$\mu_1^N(t) = B_1 \sum_{\theta} P^N(\theta) U(\theta) (\times_{v=1}^{l_n(\theta)} \mu_v(0)),$$

where B_1 is the projection on the distribution of particle 1, $\times_{v=1}^{l_n(\theta)} \mu_v(0)$ is the initial distribution on $S^{|\theta|}$ and $l_k(\theta)$ is the number of elements in the union $\bigcup_{i=n-k+1}^{n} \{v_i, w_i\}$.

It is easy to get explicit formula for P_k^N. For example, for $n=0$ that is for the empty θ we get $P_0^N=\exp(-2\lambda t)$, for $n=1$ we have

$$P_1^N=2\lambda\int\exp(-2\lambda(t-t_1))\exp\left(-2\lambda\left(2-\frac{1}{N-1}\right)t_1\right)dt_1$$

that is there is no particle 1 on the time interval (t_1,t) and there are no particles 1 and i (assuming that $\theta=(1,i)$) on the interval $(0,t_1)$. For $n=2$ we have

$$\begin{aligned}P_2^N&=\sum_{i\neq j}P(\theta_1(\omega)=(1,i),(1,j))+\sum_i P(\theta_1(\omega)=(1,i),(1,i))\\&\quad+\sum_{i\neq j}P(\theta_1(\omega)=(1,i),(i,j)),\end{aligned}$$

where, for example,

$$\begin{aligned}\sum_{i\neq j}P(\theta_1(\omega)&=(1,i),(1,j))\\&=(2\lambda)^2\frac{N-2}{N-1}\int\int\exp(-2\lambda(t-t_2))\exp\left(-2\lambda\left(2-\frac{1}{N-1}\right)(t_2-t_1)\right)\\&\quad\times\exp\left(-\frac{2\lambda}{N-1}a_3t_1\right)dt_1\,dt_2,\end{aligned}$$

where a_3 is the number of pairs, which intersect with $\{1,2,3\}$. In the general case the formula looks quite similar

$$P^N(\theta)=\left(\frac{2\lambda}{N-1}\right)^n\int\cdots\int\prod_{k=1}^n\exp(-m(N,k,\theta)\frac{2\lambda}{N-1}(t_k-t_{k-1}))dt_1\ldots dt_n,$$

where $m(N,k,\theta)$ are some positive numbers. However, we will simplify our task: we do not need exact expression for the exponents because we will use the estimates

$$\exp(-m\lambda(t_k-t_{k-1}))\leqslant 1,\ \|U(\chi)\|\leqslant 1.$$

For the integration we will use

$$\int\ldots\int dt_1\ldots dt_n=\frac{t^n}{n!}. \tag{A.1}$$

It is convenient to consider equivalence classes of connected sequences. We say that two sequences are equivalent if one can be obtained from the other by some permutation $\phi: \{1, \dots, N\} \to \{1, \dots, N\}$ of particles. Note that $m(N, k, \theta)$ and $P^N(\theta)$ depend only on the equivalence class.

Let A be a subset of $\{1, \dots, n\}$. We say that a sequence θ has type A if the pair $\{v_i, w_i\}$ is essential for any $i \in \{1, \dots, n\} \setminus A$ and non-essential otherwise. Essential sequences correspond to $A = \varnothing$. The number $C_{n,ess}^{(N)}$ of essential sequences of length n satisfies the following properties:

$$\left(\frac{1}{N-1}\right)^n C_{n,ess}^{(N)} = \prod_{k=1}^{n} k \frac{N-k}{N-1} \leqslant n!, \left(\frac{1}{N-1}\right)^n C_{n,ess}^{(N)} \to n! \tag{A.2}$$

For any non-empty A we get similarly

$$\left(\frac{1}{N-1}\right)^n C_{n,A}^{(N)} \leqslant n!, \left(\frac{1}{N-1}\right)^n C_{n,A}^{(N)} \to 0 \tag{A.3}$$

as $N \to \infty$.

We need also the evident property that $m(N, k, \theta)(1/(N-1))$ tend to some $m(k, \theta)$ as $N \to \infty$. Finally we have

$$\mu_1^N(t) = B_1 \sum_n \left(\frac{2\lambda}{N-1}\right)^n \sum_{\theta: |\theta| = n} \int \cdots \int \exp(-2\lambda m(k, \theta)(t_k - t_{k-1}))$$
$$\times dt_1 \dots dt_n \sum_{ess} U(\theta)(\mu_1(0) \times \cdots \times \mu_{l_n(\theta)}(0)).$$

By (A.3), in the limit non essential sequences do not count and we get using (A.2)

$$\mu_1(t) = B_1 \sum_n \lambda^n \sum_{\theta: |\theta| = n} \int \cdots \int \exp(-2\lambda m(k, \theta)(t_k - t_{k-1}))$$
$$\times dt_1 \dots dt_n \sum_{ess} U(\chi)(\mu_1(0) \times \cdots \times \mu_{n+1}(0)).$$

For small t the terms of both series have uniform exponentiall bounds by (A.1). Moreover, due a term-by-term convergence,

$$\mu_1(t) - \mu_1^N(t)$$

tends to zero in the norm. C^∞ dependence on t follows from this. Chaos property can be shown quite similarly.

REFERENCES

1. L. Arnold and M. Theodosopulu. Deterministic limit of the stochastic model of chemical reactions with diffusion, *Adv. Appl. Prob.* **12**:367–379 (1980).
2. M. Bramson and J. Lebowitz. Spatial structure in low dimensions for diffusion limited two-particle reactions, *Ann. Appl. Prob.* (2001).
3. Dobrushin R, On the Poisson law for the distribution of particles in space, *Ukrainian Math. J.* **8**(2):130–134 (1956).
4. G. Fayolle, V. Malyshev, and S. Pirogov, Stochastic chemical kinetics with energy parameters. Rapports de Recherche, INRIA, No. 5008, 2003. To appear in "Trends in Mathematics: Mathematics and Computer Science", v. 3, Birkhauser, 2004.
5. C. Gadgil, Chang-Hyeong Lee and H. Othmer, A stochastic analysis of first-order reaction networks. Preprint, 2003.
6. M. Kac, *Probability and Related Topics in Physical Sciences*. (Interscience Publishers, 1958).
7. J. Keizer, *Statistical Thermodynamics of Nonequilibrium Processes* (Springer, Berlin, 1987).
8. P. Kotelenez, Law of large numbers and central limit theorem for linear chemical reaction with diffusion, *Ann. Prob.* **14**:173–193 (1986).
9. L. Landay, Lifshitz, *Course of Theoretical Physics, v. 5: Statistical Physics* (Moscow, 1976) 584 pp.
10. J. Lebowitz and Ch. Maes. *Entropy—a Dialog. In "Entropy"* (Princeton Univ. Press, Princeton, 2003), pp. 269–276.
11. M. A. Leontovich, Main equations of kinetical theory of gases from the random processes point of view, *J. Experim. Theor. Physics* **5**(3–4):211–231 (1935).
12. Th. Ligget, *Interacting Particle Systems* (Springer, Berlin, 1985) 496 pp.
13. C. Maes, K. Netocny, and M, Verschuere. Heat conduction networks, *J. Stat. Phys.* **111**:1219–1244 (2003).
14. Ch. Maes and M. van Wieren, A Markov model for kinesin, JSP **112**(1/2):329–335 (2003).
15. V. Malyshev and R. Minlos, Linear infinite-particle operators, *AMS Translations Math. Monographs* **143** (1995).
16. V. Malyshev, S. Pirogov and A. Rybko. Random walks and chemical networks *Moscow Math. J.* **2** (2004).
17. A. De Masi, P. Ferrari, and J. L. Lebowitz, Reaction–diffusion equations for interacting particle systems, *J. Stat. Phys.* **44**(3/4):589–644 (1986).
18. D. McQuarrie, Stochastic approach to chemical kinetics, *J. Appl. Prob.* **4**:413–478 (1967).
19. H. Othmer, Analysis of complex reaction networks. University of Minnesota preprint, Minneapolis, December 9, 2003.
20. R. F. Streater, *Statistical Dynamics*. (Imperial College Press, 1995).
21. J. Tuszynski, M. Kurzynski, *Introduction to molecular biophysics* (CRC Press, 2003).