Stochastic modeling of the anaerobic model AM2b

Models at different scales

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ABSTRACT. The AM2B model is conventionally represented, in large population, as a system of ordinary differential equations. Our goal is to build several models at different scales. At the microscopic scale (the scale of the individual), we propose a pure jump stochastic model. This model can be exactly simulated. However, when the size of the population is large that type of exact simulation is not feasible, hence we propose approximated simulation methods in discrete time, of the Poisson type or of the diffusive type. The diffusive type of approximated simulation method can be seen as a discretization of a stochastic differential equation. Finally, we present informally a law of large numbers/central limit theorem of the functional type and how they can be used to provide models at different scales or hybrid models.

RÉSUMÉ. Le modèle AM2B est classiquement représenté, en grande population, par un système d'équations différentielles. Notre objectif est d'établir plusieurs modèles à différentes échelles. À l'échelle microscopique (individuelle), on propose un modèle stochastique de saut pur. Ce modèle peut être simulé de façon exacte. Lorsque la taille de la population est grande ce genre de simulation n'est pas praticable, et nous proposons des méthodes de simulation, à pas de temps discret, de type poissonnien ou de type diffusif. La méthode de simulation de type diffusif peut être vue comme une discrétisation d'une équation différentielle stochastique. Nous présentons enfin de façon informelle un résultat de type loi des grands nombres/théorème central limite fonctionnel et comment ce résultat peut conduire à des modèles selon l'échelle considérée ou encore à des modèles hybrides.

KEYWORDS: AM2B model, pure jump process, ordinary differential equation, diffusion approximation, stochastic differential equation

MOTS-CLÉS: modèle AM2B, processus de saut pure, équation différentielle ordinaire, approximation diffusion, équation différentielle stochastique
Stochastic models recently gain more credibility and numerical efficiency in chemistry [7], biotechnology [8], system biology [12] where deterministic models have been extensively used. Taking the example of a biotechnological model, we explain how a stochastic modeling approach deepens the insights allowed by the deterministic classical models.

Wastewater treatment plant aims at reducing the volume of pollutants rejection, producing potential energy like CH₄ in anaerobic treatment, providing treated water for agriculture and industry. Among these technologies anaerobic membrane bioReactors are promising technologies provided that membrane fouling phenomenon could be reduced. AM2b is a mathematical model of anaerobic membrane bioReactors developed by [1, 2], it is a variant of model AM2 (2-steps Acidogenesis-Methanogenesis model, see [3]) with soluble microbial products (SMP) dynamics. The production and the degradation of SMP play an important role in the membrane fouling phenomenon.

We present the original ODE model of the AM2b. Then we introduce a pure jump Markov model of the same device and a exact Monte Carlo simulation method of this process. Next we propose faster approximated simulation methods. Finally we present a stochastic differential equation (SDE) model of the AM2b. The validity of these models depends on the scale considered for the problem, this could be cleared with a law of large numbers/central limit theorem of the functional type presented in the last section.

1. The ODE model

The state variable of this model is:

\[
\begin{align*}
    x & = \begin{pmatrix}
        s_1 \\
        b_1 \\
        s_2 \\
        b_2 \\
        s
    \end{pmatrix} \\
    & \text{concentration of organic matter} \\
    & \text{concentration of acidogenic biomass} \\
    & \text{concentration of volatile fatty acids (VFA)} \\
    & \text{concentration of methanogenic biomass} \\
    & \text{concentration of the soluble microbial products (SMP)}
\end{align*}
\]

The AM2b model describes the dynamics of biological and anaerobic wastewater treatment in the following way:

\[
\begin{align*}
    Q_{in} & = Q_{in} + Q_{out} \\
    Q_{out} & = (1 - \beta) s \\
    s_{1}, s_{2}, s_{2}, (1 - \beta) s
\end{align*}
\]

On the right of these scheme the membrane fouling model is represented; the separation of matter is as follow: the substrates \( s_1 \) and \( s_2 \) go through the membrane without retention (the size of their molecules is assumed to be smaller than pore diameter), the biomass
2. Pure jump Markov model

Following the approach described in [4], we propose a representation of the AM2b model as a pure jump Markov process:

\[ X(t) = (S_1(t), B_1(t), S_2(t), B_2(t), S(t))^* \]  

(4)
taking values in \( \mathbb{R}_+^J \). This process will encompass the \( J \) reactions: each reaction \( j \) is now characterized by its intensity functions \( \lambda_j(x) \) and its jump functions \( \nu_j(x) \), see details in Section A.3. The dynamic of the process \( X(t) \) is described as follows: \( X(0) = x_0 \) and conditionally on \( X(t) = x \), we set

\[
X(t + \Delta t) = \begin{cases} 
  x + \nu_j(x) & \text{with probability } \lambda_j(x) \Delta t + o(\Delta t) \quad 1 \leq j \leq J \\
  x & \text{with probability } 1 - \sum_{j=1}^J \lambda_j(x) \Delta t + o(\Delta t)
\end{cases}
\]

(5)

where \( (\lambda_j(x), \nu_j(x))_{1 \leq j \leq J} \) is given by (12) and (13).

2.1. Simulation and representation of \( X(t) \)

The process \( X(t) \) can be simulated according to the following SSA (stochastic simulation algorithm) [6]:

\[
\begin{align*}
X & \leftarrow x_0, \quad t \leftarrow 0 \\
\text{while } t < T_{\text{max}} & \text{ do} \\
\tau & \leftarrow \sum_{j=1}^J \lambda_j(X) \\
S & \leftarrow \text{Exp}(\tau) \\
\text{sample } j & \text{ according to the distribution } (\frac{\lambda_j(X)}{S}, \ldots, \frac{\lambda_j(X)}{S}) \\
t & \leftarrow t + S \\
X & \leftarrow X + \nu_j(X) \\
\text{end while}
\end{align*}
\]

(6)

This Monte Carlo procedure allows us to simulate exact trajectories of the process \( X_t \), the only approximation resides in the algorithms used for simulating the basic probability distributions.

Algorithm (6) is an exact representation of the process \( X(t) \), and it leads to the following representation of the process:

\[
X_t = X_0 + \sum_{j=1}^J \int_{[0,t]) \times \mathbb{R}_+} 1_{[0,\lambda_j(X_s^{-})]}(v) \nu_j(X_s^{-}) \mathcal{N}_j(ds, dv)
\]

(7)

where \( \mathcal{N}_j(ds, dv) \) are independent Poisson random measures of intensity measure \( ds \times dv \) (the Lebesgue measure on \( \mathbb{R}_+^J \)).

3. Discrete time approximations

The SSA simulates each reaction of the ecosystem asynchronously in time. In many situations this detailed simulation is too cumbersome, this is why synchronous discrete time approximations have been proposed. Let \( t_m = m \Delta t \), for \( \Delta t > 0 \) fixed.

Poisson approximation

We construct an approximation \( (\tilde{X}(t_m))_{m \geq 1} \). On the interval \( [t_m, t_{m+1}) \) suppose that the different rate functions are approximated by:

\[
\lambda_j(x) \simeq \lambda_j(\tilde{X}(t_m)), \quad \forall x \in \mathbb{R}_+^J
\]

so that each of the \( J \) reactions are independent and occur at constant rates \( \lambda_j(\tilde{X}(t_m)) \), that is the number of reactions of type \( j \) is a Poisson process of intensity \( \lambda_j(\tilde{X}(t_m)) \).
Hence, on the time interval \([t_m, t_{m+1})\) the number of reactions of type \(j\) follows a Poisson distribution of parameter \(\Delta t \lambda_j(\bar{X}(t_m))\). We obtain the following approximation also called \(\tau\)-leaping:

\[
\bar{X}(t_{m+1}) = \left[ \bar{X}(t_m) + \sum_{j=1}^{J} \nu_j(\bar{X}(t_m)) \rho_{j,m} \right]_+
\]  

(8)

where \(\rho_{j,m}\) are independent Poisson distribution variables with parameter \(\Delta t \lambda_j(\bar{X}(t_m))\) and \([x]_+\) is the projection of \(\mathbb{R}^2\) onto \(\mathbb{R}^2_+\) (the positive part of each component).

**Diffusion approximation**

The Poisson distribution with parameter \(\Delta t \lambda_j(\bar{X}(t_m))\), for \(\Delta t \lambda_j(\bar{X}(t_m))\) large enough, can be approximated by a Normal distribution of mean \(\Delta t \lambda_j(\bar{X}(t_m))\) and variance \(\Delta t \lambda_j(\bar{X}(t_m))\). From (8) we get:

\[
\bar{\xi}(t_{m+1}) = \left[ \bar{\xi}(t_m) + \sum_{j=1}^{J} \nu_j(\bar{\xi}(t_m)) \left( \Delta t \lambda_j(\bar{\xi}(t_m)) + \sqrt{\Delta t \lambda_j(\bar{\xi}(t_m))} w_{j,m} \right) \right]_+
\]

where \(w_{j,m}\) are independent \(N(0,1)\) random variables. This last equation can be rewritten:

\[
\bar{\xi}(t_{m+1}) = \left[ \bar{\xi}(t_m) + F(\bar{\xi}(t_m)) \Delta t + \sum_{j=1}^{J} \frac{1}{\sqrt{N_j}} g_j(\bar{\xi}(t_m)) [W_j(t_{m+1}) - W_j(t_m)] \right]_+
\]

(9)

where \(W_j(t)\) are independent standard Brownian motions so that \(W_j(t_{m+1}) - W_j(t_m)\) are independent and \(N(0, \Delta t)\): \(F(x)\) is defined in (15) and:

\[
g_j(x) \equiv \frac{\sqrt{N_j}}{\sqrt{\lambda_j(x)}} \nu_j(x) = \sqrt{\lambda_j(x)} N_j \nu_j(x).
\]

Let

\[
\bar{g}_j(x) \equiv \sqrt{\lambda_j(x)} \tilde{\nu}_j
\]

so that:

\[
g_j(x) - \bar{g}_j(x) = 1_{x \in \mathcal{D}} \left( g_j(x) - \bar{g}_j(x) \right)
\]

and \(|g_j(x) - \bar{g}_j(x)| \leq C 1_{x \in \mathcal{D}} \sqrt{1 + |x|}.

**Stochastic differential equation**

Equation (9) is an Euler-Maruyama discrete time approximation of the following stochastic differential equation (SDE):

\[
d\xi(t) = F(\xi(t)) dt + \sum_{j=1}^{J} \frac{1}{\sqrt{N_j}} g_j(\xi(t)) dW_j(t), \quad \xi(0) = x_0.
\]

(10)
4. Scales and asymptotics

According to Section A.3, the scale parameters $N_j$ are connected to the “size” of the jumps in the reactions $\mathbb{D}$. We can assume that the $F_j$’s range from $10^4$ to $10^6$. When a reaction involves only substrate molecules the corresponding $F_j$’s range from $10^7$ to $10^9$; when a reaction involves only bacteria the corresponding $F_j$’s range from $10^4$ to $10^6$. Hence for reasonable concentrations, the simulation algorithm (6) will not be feasible as it simulates every single reaction.

First suppose that $N_j = N_j$ for all $j$ and that $N$ is large. The first well know result can be understood as a functional law of large numbers (originally proved in this context by Tom Kurtz [9, 10]), it states that:

$$\sup_{0 \leq t \leq T} |X(t) - x(t)| \xrightarrow{N \to \infty} 0$$

in $L^2$ or in probability. It is clear that in (11) we can replace $X(t)$ by $\xi(t)$. So under mild conditions, when the population sizes are large and so the number of reaction, the ODE model (2) is adapted to this scale.

At an intermediate scale, a functional central limit theorem states that the process $\beta N \left( X(t) - x(t) \right)$ can be approximated in law by $\sum_{j=1}^{J} \int T \ g_j(x(s)) \ d\bar{W}_j(s)$ where the $\bar{W}_j(s)$ are independent standard Brownian motions, that is formally:

$$X(t) \approx x(t) + \frac{1}{\sqrt{N}} \sum_{j=1}^{J} \int T \ g_j(x(s)) \ d\bar{W}_j(s).$$

This also proves that the SDE model (10) is adapted to this scale.

In many situation ODE and SDE models are not valid. This is the case when one of the bacterial population is of “small” size but still affects the global dynamic of the process. This so-called “molecular randomness” may influence the global dynamic even when the population sizes are not so small [5]. In this case we may adopt hydride approaches. We just present an example where we separate the dynamics of the substrates from the dynamics of the biomass: The idea is to break down the reactions between substrate type reactions and biomass type reactions, then to describe the first ones as a system of ODE’s and to describe the second ones as a pure jump Markov process. For example we can obtain a system of ODE’s describing the continuous evolution of the substrates and the SMP concentrations:

$$\begin{align*}
\dot{s}_1 &= D_n (S_{1n} - s_1) - k_1 \mu_1 (s_1) B_1, \\
\dot{s}_2 &= D_n (S_{2n} - s_2) - k_2 \mu_2 (s_2) B_2 + (c_{12} \mu_1 (s_1) + c_{02} \mu (s)) B_1, \\
\dot{s} &= (c_{10} \mu_1 (s_1) + D_m - k_0 \mu (s)) B_1 + (c_{20} \mu_2 (s_2) + D_m) B_2 - M \dot{s}.
\end{align*}$$

coupled to a 2-dimensional pure jump process describing the discrete evolution of the biomasses concentrations:

<table>
<thead>
<tr>
<th>Jump</th>
<th>Rate</th>
<th>Jump</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B_1 \rightarrow B_1 + s_1$</td>
<td>$\mu_1(s_1) B_1 / \delta_1$</td>
<td>$B_2 \rightarrow B_2 + s_2$</td>
<td>$\mu_2(s_2) B_1 / \delta_1$</td>
</tr>
<tr>
<td>$B_1 \rightarrow B_1 + s_1$</td>
<td>$\mu(s) B_1 / \delta_1$</td>
<td>$B_2 \rightarrow B_2 - s_2$</td>
<td>$D_n B_1 / \delta_2$</td>
</tr>
<tr>
<td>$B_1 \rightarrow B_1 - s_1$</td>
<td>$D_m B_1 / \delta_1$</td>
<td>$B_2 \rightarrow B_2 - s_2$</td>
<td>$D_n B_1 / \delta_2$</td>
</tr>
<tr>
<td>$B_1 \rightarrow B_1 - s_1$</td>
<td>$D_m B_1 / \delta_1$</td>
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</tbody>
</table>
This type of model, known as Piecewise-deterministic Markov process, is very promising and will be investigated in the near future.

5. Conclusion

We show that an ODE model of microbial dynamics (1) contains all the ingredients that can be used to establish a pure jump Markov model, see Section 2. This pure jump Markov model can be exactly simulated with the Monte Carlo technique (6). This exact Monte Carlo method is not feasible in large population size cases and we proposed a Poissonian discrete time approximation (8) (also called τ-leaping) and a diffusion discrete time approximation (9). This last equation is the Euler-Maruyama time discretization of the SDE (10). This SDE is valid in high population size and different recalling so that alternative formulations of this SDE can be established. In Section 4, we describe the validity of these different models according to the scales at which the process should be simulated. All these models share the same ingredient, however the have very different qualitative properties.

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6. References


A. Appendix: the AMB2b models

A.1. AMB2b as a reaction network

The first set of reactions describes the biochemical reactions:

- **Acidogenesis and SMP production**
  \[ \circ S_1 + B_1 \xrightarrow{r_1} 2 B_1 + c_{12} S_2 + c_{10} S \]
- **Methanogenesis and SMP production**
  \[ \circ S_2 + B_2 \xrightarrow{r_2} 2 B_2 + c_{20} S \]
- **SMP degradation**
  \[ \circ S_0 + B_1 \xrightarrow{r_3} 2 B_1 + c_{02} S_2 \]
- **SMP production from biomass decay**
  \[ B_1 \xrightarrow{r_4} S \quad \circ B_2 \xrightarrow{r_5} S \]

The second set of reactions describes the substrate inflow and the substrate outflow through the membrane:

\[ \circ \emptyset \xrightarrow{r_6} S_1 \quad \circ \emptyset \xrightarrow{r_7} S_2 \quad \circ S_1 \xrightarrow{r_8} \emptyset \quad \circ S_2 \xrightarrow{r_9} \emptyset \quad \circ S \xrightarrow{r_{10}} \emptyset \]

The third and last set of reactions describes the biomass and substrate withdrawal with:

\[ \circ S_1 \xrightarrow{r_{11}} \emptyset \quad \circ S_2 \xrightarrow{r_{12}} \emptyset \quad \circ S \xrightarrow{r_{13}} \emptyset \quad \circ B_1 \xrightarrow{r_{14}} \emptyset \quad \circ B_2 \xrightarrow{r_{15}} \emptyset \]

The second and third set of reactions are not biochemical reactions they just describe the inflows and outflows in the AM2B process. In reaction \( \circ \) only a proportion \( \beta \) of the SMP goes through the membrane, and in reaction \( \circ \) a proportion \( 1 - \beta \) of the SMP is withdrawn, this mechanism will be explicated in the definition of the rates. Let \( j \) the index of the reaction and \( J = 15 \) the number of reactions. \( \{ (\circ, r_j); j = 1, \ldots, J \} \)

A.2. AMB2b as an ODE system

The AMB2b reaction network described in Section A.1 is "translated" to an ODE system thanks to the laws of mass action and conservation of mass. The state variables of the ODE system are the concentrations \( s_i = |S_i|, b_i = |B_i| \) \( i = 1, 2 \) and \( s = |S| \). For example, for the \( \circ \), the rate of reaction also called speed of reaction, is defined by:

\[ r_1 = \frac{b_1(t + \Delta t) - b_1(t)}{\Delta t} = -k_1 \frac{s_1(t + \Delta t) - s_1(t)}{\Delta t} = c_{12} \frac{s_2(t + \Delta t) - s_2(t)}{\Delta t} = c_{10} \frac{a(t + \Delta t) - a(t)}{\Delta t} \]

(the equalities are due to the mass conservation). This reaction, like reactions \( \circ \) and \( \circ \), is of order two and the mass action law states that \( r_1 = s_1 b_1 \), but saturation/inhibition phenomena suggest to replace in this last expression \( s_1 \) by \( \mu_1(s_1) \) indeed:

**Biochemical reactions:** The mass action law applied to the second order reactions \( \circ \circ \circ \) states that:

\[ r_1 = \mu_1(s_1) b_1, \quad r_2 = \mu_2(s_2) b_2, \quad r_3 = \mu(s) b_1 \]

where the growth functions \( \mu_i \) and \( \mu \) are chosen as (3), indeed for low substrate concentration, these growth functions are linear accordingly to the mass action law, but for higher
substrate concentrations, saturation and inhibition phenomena have to be taken into account. The mass action law applied to first order reactions \( \circ \circ \) gives \( r_4 = D_{m} b_1 \) and \( r_5 = D_{m} b_2 \) where \( D_{m} \) is decay rate of biomass.

**Inflow and outflows:** Inflow is done at rate \( D_{in} \), outflow though the membrane at rate \( D_{or} \) and only a proportion \( \beta \) of the SMP is affected by the outflow, so the rates of these reactions are:

\[
\begin{align*}
    r_6 &= D_{in} S_{in}, & r_7 &= D_{or} S_{or}, & r_8 &= D_{or} S_{1}, & r_9 &= D_{or} S_{2}, & r_{10} &= \beta D_{or} s. 
\end{align*}
\]

**Withdrawal:** The withdrawal is done at rate \( D_{w} \), and only a proportion \( 1 - \beta \) of the SMP affected by the withdrawal, so the rates of these reactions are:

\[
\begin{align*}
    r_{11} &= D_{w} s, & r_{12} &= D_{w} s, & r_{13} &= (1 - \beta) D_{w} s, & r_{14} &= D_{w} b_1, & r_{15} &= D_{w} b_2. 
\end{align*}
\]

Summing up these expressions and applying the mass conservation law lead to the system of differential equations (1).

### A.3. AMB2b as a pure jump Markov process

The AMB2b reaction network described in Section A.1 is “translated” into a pure jump Markov process thanks to the stochastic law of mass action [12]. Now \( X(t) = [S_1(t), B_1(t), S_2(t), B_2(t), S(t)]^T \) is a pure jump Markov process defined by (5) where each reaction \( \circ \circ \) is described as an instantaneous jump \( X(t) \rightarrow X(t) + \nu_j(X(t)) \) occurring with intensity \( \lambda_j(X(t)) \) defined respectively by:

\[
\lambda_j(x) \overset{\text{def}}{=} N_j \dot{\lambda}_j(x), \quad \nu_j(x) \overset{\text{def}}{=} [x + \frac{1}{N_j} \nu_j(x)] - x \tag{12}
\]

\( \langle x \rangle \), the orthogonal projection of \( x \) into \( \mathbb{R}_{+}^{5} \) with

\[
\begin{array}{cccccc}
    & j & \lambda_j(x) & \nu_j(x) \\
\hline
\circ & 1 & \mu_1 S_{1} b_1 & -k_1 & +1 & +c_{12} & 0 & +c_{10} \\
\circ & 2 & \mu_2 S_{2} b_2 & 0 & 0 & -k_2 & -1 & +c_{20} \\
\circ & 3 & \mu_{or} s & 0 & +1 & +c_{02} & 0 & -k_0 \\
\circ & 4 & D_{w} S_{1} & 0 & -1 & 0 & 0 & +1 \\
\circ & 5 & D_{w} S_{2} & 0 & 0 & 0 & 0 & -1 \\
\circ & 6 & D_{w} s & 0 & 0 & 0 & 0 & -1 \\
\circ & 7 & \beta D_{or} s & 0 & 0 & 0 & 0 & -1 \\
\circ & 8 & D_{or} s & 0 & 0 & 0 & 0 & -1 \\
\circ & 9 & D_{or} b_1 & 0 & 0 & 0 & 0 & -1 \\
\circ & 10 & D_{or} b_2 & 0 & 0 & 0 & 0 & -1 \\
\circ & (1 - \beta) D_{w} s & 0 & 0 & 0 & 0 & -1 \\
\end{array}
\tag{13}
\]

**About the second equation of (12):** Basically the jumps are \( \frac{1}{N_j} \nu_j(x) \), but near the border of \( \mathbb{R}^5_{+} \) to avoid jumps that can lead to negative concentration values, we adopt truncated jumps so that \( x + \nu_j(x) \in \mathbb{R}^5_{+} \) for all \( x \in \mathbb{R}^5_{+} \). Indeed, note that \( -\tilde{v}_{ij} \leq \tilde{v}_{ij} \leq \tilde{v}_{ij} \), so that if \( x_i \geq \tilde{v}_{ij} \min_j N_j \) then \( \nu_j(x) = \tilde{v}_{ij} N_j \), where \( \tilde{v}_{ij} \) and \( \nu_j(x) \) denote the \( i \)th component of \( \nu_j \) and \( \nu_j(x) \) respectively. Define:

\[
\mathcal{D} \overset{\text{def}}{=} \{ x \in \mathbb{R}^5_{+} ; x_i \geq \tilde{v}_{ij} \min_j N_j \} \tag{14}
\]
so that \( x \in \mathcal{D} \) implies that \( \nu_j(x) = \frac{1}{N_j} \tilde{\nu}_j \).

**The drift coefficient:** Given \( X(t) = x \), the expectation of \( X(t + \Delta t) \) is

\[
\mathbb{E}[X(t + \Delta t)|X_t = x] = \sum_{j=1}^{J} (x + \nu_j) \mathbb{P}[^{\text{reaction } j}|X_t = x] + x \mathbb{P}[\text{no reaction } |X_t = x]
\approx \sum_{j=1}^{J} (x + \nu_j) (\lambda_j(x) \Delta t) + x (1 - \sum_{j=1}^{J} \lambda_j(x) \Delta t)
\approx x + \sum_{j=1}^{J} \lambda_j(x) \nu_j(x) \Delta t = x + F(x) \Delta t
\]

where

\[
F(x) \triangleq \sum_{j=1}^{J} \lambda_j(x) \nu_j(x) \tag{15}
\]

So locally in time, \( \mathbb{E}(X(t)) \) evolves according to the drift coefficient \( F(x) \) (note that \( \mathbb{E}(X(t)) \) is not solution of an ODE as the function \( F \) is non linear). We can easily check that:

\[
F(x) = 1_{x \in \mathcal{D}} \tilde{F}(x) + 1_{x \notin \mathcal{D}}(x) F(x)
\]

where

\[
F(x) \triangleq \sum_{j=1}^{J} \tilde{\lambda}_j(x) \tilde{\nu}_j \tag{16}
\]

does not depend on the \( N_j \)’s. Finally from \(|F(x)| + |\tilde{F}(x)| \leq C (1 + |x|)\) and \( F(x) - \tilde{F}(x) = 1_{x \notin \mathcal{D}}(F(x) - \tilde{F}(x)) \), we get:

\[
|F(x) - \tilde{F}(x)| \leq C 1_{x \notin \mathcal{D}}(1 + |x|).
\]