



Arithmetic Subderivatives Relative to Subsets of Primes

Champak Talukdar^{*1,2} and Helen K. Saikia²

¹Department of Mathematics, Behali Degree College, Bargang, Sukan Suti 784167, Assam, India

²Department of Mathematics, Gauhati University, Gauhati 781014, Assam, India

*Corresponding author: champak.nlb.2012@gmail.com

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Abstract. The *arithmetic derivative* is a number-theoretic function that behaves analogously to differentiation defined on integers. In this paper, we extend the concept to *generalized arithmetic subderivatives* with respect to a chosen set of primes. Inspired by the work of P. Haukkanen (Generalized arithmetic subderivative, *Notes on Number Theory and Discrete Mathematics* **25**(2) (2019), 1 – 7), we introduce a family of arithmetic functions that generalize the prime-power exponents in the classical definition. We establish necessary and sufficient conditions under which these generalized subderivatives satisfy analogs of linearity, the Leibniz rule (product rule), and multiplicativity. Several illustrative examples are worked out to demonstrate the computations and properties of these subderivatives.

Keywords. Arithmetic subderivative, Multiplicative functions, Bijections, Prime powers

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1. Introduction

The arithmetic derivative $D(n)$ of a positive integer n was first introduced by Barbeau [1] as an integer-valued function satisfying properties analogous to those of differentiation. In particular, the arithmetic derivative is defined by the rules $D(p) = 1$ for each prime p , and $D(ab) = aD(b) + bD(a)$, for all positive integers a, b . These rules imply, for example, that $D(p^k) = k p^{k-1}$, for any prime power. Various properties and extensions of $D(n)$ have since been studied (see, e.g., Merikoski *et al.* [9], Ufnarovski and Åhlander [12], Haukkanen *et al.* [5, 10], and Tossavainen *et al.* [11]). One such extension is the *arithmetic partial derivative* $D_p(n)$,

introduced by Kovič [7] and Haukkanen *et al.* [8], which differentiates n with respect to a single prime p . The partial derivative $D_p(n)$ obeys the same Leibniz (product) rule, but only accounts for the contributions of the prime p in n 's factorization.

More recently, the concept of an *arithmetic subderivative* has been formulated to generalize partial derivatives to an arbitrary subset of primes. Given a nonempty set of primes S , the arithmetic subderivative $D_S(n)$ of n with respect to S is defined by [9],

$$D_S(n) = n \sum_{p \in S} \frac{v_p(n)}{p},$$

where $v_p(n)$ denotes the exponent of the prime p in the prime factorization of n . In other words, if

$$n = \prod_{p \in \mathcal{P}} p^{v_p(n)}$$

is the prime factorization of n (with \mathcal{P} the set of all primes and all but finitely many $v_p(n) = 0$), then $D_S(n)$ sums the '*partial*' contributions of primes in S towards the arithmetic derivative. Notably, $D_{\mathcal{P}}(n)$ coincides with the ordinary arithmetic derivative $D(n)$, and $D_{\{p\}}(n) = D_p(n)$ recovers the partial derivative with respect to a single prime (Kovič [7]).

P. Haukkanen [3] further generalized this idea by replacing the specific exponent function $v_p(n)$ with an arbitrary arithmetic function. In this paper, we develop the theory of these *generalized arithmetic subderivatives*. We derive characterizations for when such generalized subderivatives mimic the behavior of linear operators or derivations (obeying the Leibniz rule), and when they preserve multiplicative structures. In Section 2, we formalize definitions and recall relevant concepts of additive and multiplicative arithmetic functions. Section 3 presents the main results, including several theorems with proofs. Section 4 provides illustrative examples of calculations and verifies the theoretical results in concrete cases.

2. Preliminaries and Definitions

Throughout this paper, let \mathcal{P} denote the set of all prime numbers. For each $n \in \mathbb{N}$ (the set of positive integers), the prime factorization is written as

$$n = \prod_{p \in \mathcal{P}} p^{v_p(n)},$$

where each $v_p(n)$ is a nonnegative integer and $v_p(n) = 0$, for all but finitely many primes p . We call $v_p(n)$ the *p-adic order* of n , i.e., the exponent of prime p in n . By convention, $v_p(1) = 0$, for all p .

Definition 2.1. Let $S \subseteq \mathcal{P}$ be a nonempty set of primes. The *arithmetic subderivative of n with respect to S* is defined as

$$D_S(n) = n \sum_{p \in S} \frac{v_p(n)}{p}.$$

More generally, for each prime $p \in S$, let $f_p : \mathbb{N} \rightarrow \mathbb{C}$ be an arithmetic function such that $f_p(n) \neq 0$ for only finitely many primes p . The *generalized arithmetic subderivative with respect to S (and function collection $f = (f_p)_{p \in S}$)* is defined by

$$D_S^f(n) = n \sum_{p \in S} \frac{f_p(n)}{p}.$$

We call each f_p the *coefficient function* associated with prime p in the derivative. For brevity, we denote

$$H(n) = \sum_{p \in S} \frac{f_p(n)}{p},$$

so that $D_S^f(n) = nH(n)$.

Examples. (i) If we choose $f_p(n) = v_p(n)$ for every $p \in S$, then $D_S^f(n)$ reduces to the standard subderivative $D_S(n)$. In particular, if $S = \mathcal{P}$ and $f_p(n) = v_p(n)$ for all p , we recover $D_{\mathcal{P}}^f(n) = D(n)$, the usual arithmetic derivative (Barbeau [1], Merikoski *et al.* [9]).

(ii) If $S = \{p\}$ is a singleton set, $D_{\{p\}}^f(n) = \frac{f_p(n)}{p}n$ can be viewed as a *generalized arithmetic partial derivative* with respect to the prime p . For example, taking $S = \{2\}$ and $f_2(n) = v_2(n)$ gives $D_{\{2\}}(n) = \frac{v_2(n)}{2}n$, which only differentiates the 2-adic part of n .

We will make use of standard concepts from the theory of arithmetic functions. An arithmetic function $g(n)$ (a function $g: \mathbb{N} \rightarrow \mathbb{C}$) is said to be:

- *multiplicative* if $g(1) = 1$ and $g(mn) = g(m)g(n)$, whenever $\gcd(m, n) = 1$.
- *completely multiplicative* if $g(1) = 1$ and $g(mn) = g(m)g(n)$, for all $m, n \in \mathbb{N}$.
- *additive* if $g(mn) = g(m) + g(n)$, whenever $\gcd(m, n) = 1$.
- *completely additive* if $g(mn) = g(m) + g(n)$, for all $m, n \in \mathbb{N}$.

These definitions are classical (see, e.g., Barbeau [1], McCarthy [8], and Sivaramakrishnan [10]). For example, the function $g(n) = \ln n$ (logarithm of n) is completely additive, and the function $g(n) = n^\alpha$ (for a fixed constant α) is completely multiplicative.

Using this terminology, note that the p -adic order $v_p(n)$ is a completely additive function in n for any fixed prime p , since $v_p(mn) = v_p(m) + v_p(n)$ holds for all m, n . Consequently, the classical arithmetic derivative $D(n)$ has the fundamental property of being a *derivation* on the multiplicative monoid of positive integers; it satisfies

$$D(mn) = mD(n) + nD(m),$$

for all m, n . We investigate the conditions under which the generalized subderivative $D_S^f(n)$ enjoys this and other properties.

3. Main Results

In what follows, assume $S \subseteq \mathcal{P}$ is fixed and that $D_S^f(n)$ is defined as above via a collection $\{f_p\}_{p \in S}$. We first characterize when D_S^f acts as a derivation (satisfies the Leibniz rule). We then examine its behavior with respect to addition and scalar multiplication, and finally its multiplicative properties. This concept is closely related to the study of Leibniz-additive functions, which continues to be an active area of research (Haukkanen *et al.* [5]).

Theorem 3.1 (Leibniz Rule). *The generalized arithmetic subderivative D_S^f satisfies the Leibniz rule*

$$D_S^f(mn) = mD_S^f(n) + nD_S^f(m),$$

for all positive integers m, n if and only if the function $H(n)$ is completely additive.

Proof. (\Rightarrow): Assume D_S^f satisfies $D_S^f(mn) = mD_S^f(n) + nD_S^f(m)$, for all m, n . By the definition $D_S^f(x) = xH(x)$, this condition expands to:

$$mnH(mn) = m(nH(n)) + n(mH(m)).$$

Simplifying, we cancel the factor mn (which is nonzero) to obtain:

$$H(mn) = H(m) + H(n).$$

This holds for all $m, n \in \mathbb{N}$, hence H is completely additive.

(\Leftarrow): Conversely, assume H is completely additive, i.e., $H(mn) = H(m) + H(n)$ for all m, n . Then for any m, n ,

$$mD_S^f(n) + nD_S^f(m) = m(nH(n)) + n(mH(m)) = mn(H(n) + H(m)).$$

By complete additivity of H , $H(n) + H(m) = H(mn)$. Thus $mD_S^f(n) + nD_S^f(m) = mnH(mn) = D_S^f(mn)$. This confirms the Leibniz rule. \square

Corollary 3.2. For a single prime p , the generalized partial derivative $D_{\{p\}}^f(n) = \frac{f_p(n)}{p}n$ satisfies $D_{\{p\}}^f(mn) = mD_{\{p\}}^f(n) + nD_{\{p\}}^f(m)$ for all m, n , if and only if $\frac{f_p(n)}{p}$ is a completely additive function of n .

Proof. In the case $S = \{p\}$, the condition from Theorem 3.1 is that $H(n) = \frac{f_p(n)}{p}$ is completely additive. This is equivalent to $f_p(n)$ itself being completely additive (since p is a constant factor). The claim follows directly. \square

Next, we turn to the additive and homogeneous properties of D_S^f . In general, the arithmetic derivative $D(n)$ is *neither* an additive function in the sense of $D(m+n) = D(m) + D(n)$, *nor* homogeneous ($D(kn) = kD(n)$ in general). We find that the generalized subderivative can exhibit these properties only in degenerate cases.

Theorem 3.3 (Additivity and Homogeneity). Suppose D_S^f satisfies

$$D_S^f(m+n) = D_S^f(m) + D_S^f(n), \quad \text{whenever } \gcd(m, n) = 1,$$

and also

$$D_S^f(an) = aD_S^f(n), \quad \text{whenever } \gcd(a, n) = 1.$$

Then, $H(n)$ must be a constant function. Conversely, if $H(n) \equiv C$ is constant for all n , then $D_S^f(n) = Cn$ is a linear function of n that trivially satisfies both properties for all m, n .

Proof. First, suppose $D_S^f(m+n) = D_S^f(m) + D_S^f(n)$, whenever $\gcd(m, n) = 1$. Taking $n = 1$ (which is coprime with every m), we have

$$(m+1)H(m+1) = D_S^f(m+1) = D_S^f(m) + D_S^f(1) = mH(m) + H(1).$$

Rearrange to $(m+1)H(m+1) - mH(m) = H(1)$. By induction on m , one can solve this difference equation: for $m = 1$ it gives $H(2) = H(1)$. Assuming $H(m) = H(1)$, the step to $m+1$ yields $(m+1)H(m+1) - mH(m) = H(1)$, i.e., $(m+1)H(m+1) - mH(1) = H(1)$. Hence $H(m+1) = H(1)$. By induction, $H(m) = H(1)$ for all m . Therefore, $H(n)$ is a constant, say $H(n) \equiv C$ for some constant $C = H(1)$.

Next, assume $D_S^f(an) = aD_S^f(n)$, whenever $\gcd(a, n) = 1$. Again choose $n = 1$: then for any a coprime with 1 (i.e., any a), we have $D_S^f(a) = aD_S^f(1)$, so $aH(a) = aH(1)$. Thus $H(a) = H(1)$, for all a . In either approach, $H(n)$ is constant (say $H(n) \equiv C$).

Conversely, if $H(n) \equiv C$ is constant, then $D_S^f(n) = Cn$. In that case, $D_S^f(m+n) = C(m+n) = Cm + Cn = D_S^f(m) + D_S^f(n)$ and $D_S^f(an) = C(an) = a(Cn) = aD_S^f(n)$, for all m, n, a , thus both properties hold globally. \square

Corollary 3.4. *If all coefficient functions $f_p(n)$ are constant functions (say $f_p(n) = c_p$, for some constants c_p and all n), then $H(n) = \sum_{p \in S} \frac{c_p}{p}$ is a constant. In this case, $D_S^f(n) = \left(\sum_{p \in S} \frac{c_p}{p} \right) n$, which clearly satisfies the additivity and homogeneity for all integers.*

Remark 3.1. The additivity and homogeneity conditions in Theorem 3.3 were assumed only for coprime arguments (which is a natural restriction in number theory contexts). In fact, if $H(n)$ is constant, $D_S^f(n) = Cn$ satisfies $D_S^f(m+n) = D_S^f(m) + D_S^f(n)$ and $D_S^f(an) = aD_S^f(n)$ for all m, n, a , without any coprimality assumptions. The necessity of H being constant, however, required only the restricted conditions as stated.

Finally, we characterize when the generalized subderivative yields a multiplicative arithmetic function. Recall that a function $F(n)$ is multiplicative if $F(1) = 1$ and $F(mn) = F(m)F(n)$, for $\gcd(m, n) = 1$. Generally, the standard arithmetic derivative $D(n)$ is far from multiplicative (for instance, $D(6) = 5$, $D(2) = 1$, $D(3) = 1$, yet $5 \neq 1 \cdot 1$). For D_S^f to be multiplicative, the structural condition is as follows.

Theorem 3.5 (Multiplicativity). *The generalized subderivative $D_S^f(n)$ defines a multiplicative function (i.e., $D_S^f(1) = 1$ and $D_S^f(mn) = D_S^f(m)D_S^f(n)$, whenever $\gcd(m, n) = 1$) if and only if $H(n)$ is a multiplicative function.*

Proof. First, note that $D_S^f(1) = 1 \cdot H(1) = H(1)$. For D_S^f to be multiplicative we require $D_S^f(1) = 1$, so it is necessary that $H(1) = 1$. Now assume $\gcd(m, n) = 1$. Then

$$D_S^f(mn) = mnH(mn),$$

while

$$D_S^f(m)D_S^f(n) = (mH(m))(nH(n)) = mnH(m)H(n).$$

For these to be equal for all coprime m, n , we must have $H(mn) = H(m)H(n)$ under $\gcd(m, n) = 1$, that is exactly the condition that H is multiplicative. Conversely, if H is multiplicative (and in particular $H(1) = 1$), then $D_S^f(1) = 1 \cdot H(1) = 1$, and for any coprime m, n :

$$D_S^f(mn) = mnH(mn) = mnH(m)H(n) = (mH(m))(nH(n)) = D_S^f(m)D_S^f(n).$$

Thus, D_S^f is multiplicative. \square

Remark 3.2. In the special case $S = \{p\}$, Theorem 3.5 implies that $D_{\{p\}}^f(n) = \frac{f_p(n)}{p}n$ is multiplicative if and only if $H(n) = \frac{f_p(n)}{p}$ is multiplicative. Equivalently, $f_p(n)$ satisfies

$$H(mn) = H(m)H(n), \quad \text{for all coprime } m, n,$$

i.e.,

$$\frac{f_p(mn)}{p} = \frac{f_p(m)}{p} \cdot \frac{f_p(n)}{p}.$$

Clearing the fractions, this is

$$f_p(mn) = \frac{1}{p} f_p(m) f_p(n), \quad \text{for all coprime } m, n, \text{ with } f_p(1) = p.$$

In other words, $f_p(n)$ is a *quasimultiplicative* arithmetic function: $p \cdot f_p(mn) = f_p(m) f_p(n)$, for coprime m, n , and $f_p(1) = p$. Equivalently, $\frac{1}{p} f_p(n)$ is a multiplicative function. This observation aligns with the findings by Haukkanen [3].

4. Illustrative Examples

We present a few examples to illustrate the computations of $D_S^f(n)$ in special cases and to verify the theoretical conditions derived above.

Example 4.1 (Standard Arithmetic Derivative). Take $S = \mathcal{P}$ (all primes) and $f_p(n) = v_p(n)$, for each p . Then $D_{\mathcal{P}}^f(n) = n \sum_{p|n} \frac{v_p(n)}{p}$, which is exactly the classic arithmetic derivative $D(n)$.

As a concrete calculation, let $n = 36$. The prime factorization is $36 = 2^2 \cdot 3^2$, consequently $v_2(36) = 2$, $v_3(36) = 2$, and $v_p(36) = 0$ for other primes p . Therefore,

$$D(36) = 36 \left(\frac{v_2(36)}{2} + \frac{v_3(36)}{3} \right) = 36 \left(\frac{2}{2} + \frac{2}{3} \right) = 36 \left(1 + \frac{2}{3} \right) = 36 \cdot \frac{5}{3} = 60.$$

This can be verified using the Leibniz rule as well: for instance, $36 = 4 \cdot 9$ with $\gcd(4, 9) = 1$. We find $D(4) = 4 \left(\frac{v_2(4)}{2} \right) = 4 \left(\frac{2}{2} \right) = 4$ and $D(9) = 9 \left(\frac{v_3(9)}{3} \right) = 9 \left(\frac{2}{3} \right) = 6$. The Leibniz rule predicts $D(36)$ should equal $4D(9) + 9D(4) = 4(6) + 9(4) = 24 + 36 = 60$, confirming the calculation. As expected, $H(n) = \sum_p \frac{v_p(n)}{p}$ in this case is *not* multiplicative (for example, $H(2) = \frac{1}{2}$, $H(3) = \frac{1}{3}$, and $H(6) = H(2 \cdot 3) = \frac{1}{2} + \frac{1}{3} = \frac{5}{6}$, while $H(2)H(3) = \frac{1}{2} \cdot \frac{1}{3} = \frac{1}{6}$). Accordingly, $D(n)$ is not multiplicative. However, each $v_p(n)$ is completely additive, hence $H(n)$ is completely additive; indeed $H(mn) = H(m) + H(n)$ holds for all m, n because adding exponents corresponds to multiplying numbers. This guarantees that $D(n)$ satisfies the Leibniz rule for all m, n , as we used.

Example 4.2 (Subderivative with Restricted Prime Set). Let $S = \{2, 3\}$ and choose $f_2(n) = v_2(n)$, $f_3(n) = v_3(n)$. Then $D_S^f(n) = n \left(\frac{v_2(n)}{2} + \frac{v_3(n)}{3} \right)$ is the arithmetic subderivative of n with respect to primes 2 and 3. This derivative ignores any other prime factors of n . For instance, consider $n = 60$. We have $60 = 2^2 \cdot 3^1 \cdot 5^1$, so $v_2(60) = 2$, $v_3(60) = 1$, $v_5(60) = 1$, and $v_p(60) = 0$, for $p > 5$. Then

$$D_{\{2,3\}}(60) = 60 \left(\frac{v_2(60)}{2} + \frac{v_3(60)}{3} \right) = 60 \left(\frac{2}{2} + \frac{1}{3} \right) = 60 \left(1 + \frac{1}{3} \right) = 60 \cdot \frac{4}{3} = 80.$$

By contrast, the full arithmetic derivative $D(60)$ would include the prime 5 as well: $D(60) = 60 \left(\frac{2}{2} + \frac{1}{3} + \frac{1}{5} \right) = 60 \left(\frac{4}{3} + \frac{1}{5} \right) = 60 \left(\frac{20+3}{15} \right) = 60 \cdot \frac{23}{15} = 92$. Thus, $D_{\{2,3\}}(60) = 80$ is smaller, reflecting the omission of the 5-component. In general, $D_S(n) + D_{\mathcal{P} \setminus S}(n) = D(n)$ since one can split the sum of $\frac{v_p(n)}{p}$ over $p \in S$ and $p \notin S$. The function

$$H(n) = \frac{v_2(n)}{2} + \frac{v_3(n)}{3}$$

in this example is still completely additive (because v_2 and v_3 are individually completely additive). Therefore, $D_{\{2,3\}}(n)$ also satisfies the product rule for all m, n . For instance, taking $m = 4$, $n = 9$ (as before, $\gcd(4, 9) = 1$), we have $D_{\{2,3\}}(4) = 4\left(\frac{v_2(4)}{2} + \frac{v_3(4)}{3}\right) = 4\left(\frac{2}{2} + 0\right) = 4$, $D_{\{2,3\}}(9) = 9\left(0 + \frac{2}{3}\right) = 6$, and indeed $D_{\{2,3\}}(36) = 60$ equals $4(6) + 9(4) = 24 + 36 = 60$. In other words, whenever m and n have no prime factors outside $\{2, 3\}$, the Leibniz rule holds perfectly for $D_{\{2,3\}}(mn)$. If m or n includes other primes, the product rule can fail because those prime contributions do not get properly differentiated by $D_{\{2,3\}}$. This is consistent with our theory: $H(n)$ is completely additive, accordingly the Leibniz rule holds universally; if we had chosen a scenario where H was only additive for coprime arguments but not completely additive, the Leibniz rule would break when primes overlap (see Example 4.3).

Example 4.3 (Generalized Derivative with Non-additive Coefficients). Consider $S = \mathcal{P}$ and define $f_p(n) = \mathbf{1}_{p|n}$ (the indicator that prime p divides n). In other words, for each prime p , let

$$f_p(n) = \begin{cases} 1, & \text{if } v_p(n) \geq 1, \\ 0, & \text{if } v_p(n) = 0, \end{cases}$$

so that $f_p(n)$ simply flags the presence of p in the factorization of n . Then, the generalized subderivative is

$$D_{\mathcal{P}}^f(n) = n \sum_{p|n} \frac{1}{p}.$$

For example, $D_{\mathcal{P}}^f(8) = 8\left(\frac{1}{2}\right) = 4$, $D_{\mathcal{P}}^f(9) = 9\left(\frac{1}{3}\right) = 3$; $D_{\mathcal{P}}^f(6) = 6\left(\frac{1}{2} + \frac{1}{3}\right) = 5$. Here $H(n) = \sum_{p|n} \frac{1}{p}$ is additive for coprime arguments but *not* completely additive. For instance, $H(8) = \frac{1}{2}$ and $H(4) = \frac{1}{2}$, but $H(4) + H(2) = 1 \neq H(8)$. In accordance with Theorem 3.1, this means $D_{\mathcal{P}}^f(n)$ satisfies the Leibniz rule for products of coprime numbers, but not in general. Take $8 = 2 \cdot 4$ (which are not coprime). We find $D_{\mathcal{P}}^f(2) = 2\left(\frac{1}{2}\right) = 1$ and $D_{\mathcal{P}}^f(4) = 4\left(\frac{1}{2}\right) = 2$. The Leibniz rule requires $D_{\mathcal{P}}^f(8) = 2D_{\mathcal{P}}^f(4) + 4D_{\mathcal{P}}^f(2) = 2(2) + 4(1) = 8$. However, our direct calculation gave $D_{\mathcal{P}}^f(8) = 4$. The discrepancy arises precisely because H was not completely additive. On the other hand, if we test the rule on coprime factors, say $6 = 2 \cdot 3$, we have $D_{\mathcal{P}}^f(6) = 5$, $D_{\mathcal{P}}^f(2) = 1$, $D_{\mathcal{P}}^f(3) = 1$, and $2D_{\mathcal{P}}^f(3) + 3D_{\mathcal{P}}^f(2) = 2(1) + 3(1) = 5$, which matches $D_{\mathcal{P}}^f(6)$. This example underscores the necessity of the complete additivity condition in Theorem 3.1.

It is also interesting to note the behavior with respect to multiplicativity: $H(n) = \sum_{p|n} \frac{1}{p}$ is *not* multiplicative (for example, $H(6) = \frac{5}{6}$ vs. $H(2)H(3) = \frac{1}{2} \cdot \frac{1}{3} = \frac{1}{6}$). Accordingly, $D_{\mathcal{P}}^f(n)$ is not a multiplicative function. Indeed $D_{\mathcal{P}}^f(1) = 1\left(\sum_{p|1} \frac{1}{p}\right) = 0$, which already violates the requirement $D_{\mathcal{P}}^f(1) = 1$ for multiplicativity (no surprise, since here $f_p(1) = 0$, for all p so $H(1) = 0$).

5. Concluding Remarks and Open Problems

We have developed a theory of generalized arithmetic subderivatives that encompasses the classical arithmetic derivative and various partial and subderivative constructions. The results here, inspired by Haukkanen's work [3], provide a foundation, but many questions remain open. As research continues, we expect to see deeper connections with classical number theoretic functions and perhaps new insights into the structure of the integers through the lens

of ‘arithmetic calculus’. We outline a few natural directions for further research:

- *Other number systems*: Extend the concept to different algebraic settings. For instance, define analogous subderivatives in the ring of Gaussian integers (where primes are Gaussian primes), or over polynomial rings over finite fields (with irreducible polynomials playing the role of primes), a direction that has seen recent progress in p -adic fields and number fields (Emmons and Xiao [2]).
- *Arithmetic differential equations*: Explore connections with arithmetic differential equations. Since D_S^f behaves like a derivation under certain conditions, one could study functional equations involving D_S^f (analogous to differential equations) or dynamical systems defined by these subderivatives.

Competing Interests

The authors declare that they have no competing interests.

Authors’ Contributions

All the authors contributed significantly in writing this article. The authors read and approved the final manuscript.

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